

FIG. 1

Sequence of human APRIL (SEQ ID NOS: 1 and 2)

Human G70 cDNA (SEQ ID NO 1)

Length: 1465 bp

```

  1  GCCAACCTTC CCTCCCCAA CCCTGGGGCC GCCCCAGGGT TCCTGCGCAC
 51  TGCCTGTTCC TCCTGGGTGT CACTGGCAGC CCTGTCCTTC CTAGAGGGAC
101  TGGAACCTAA TTCTCCTGAG GCTGAGGGAG GGTGGAGGGT CTCAAGGCCAA
151  CGCTGGCCCC ACGACGGAGT GCCAGGAGCA CTAACAGTAC CCTTAGCTTG
201  CTTTCCTCCT CCCTCCTTTT TATTTTCAAG TTCCTTTTTA TTTCTCCTTG
251  CGTAACAACC TTCTTCCCTT CTGCACCACT GCCCGTACCC TTACCCGCCC
301  CGCCACCTCC TTGCTACCCC ACTCTTGAAA CCACAGCTGT TGGCAGGGTC
351  CCCAGCTCAT GCCAGCCTCA TCTCCTTTCT TGCTAGCCCC CAAAGGGCCT
401  CCAGGCAACA TGGGGGGGCC AGTCAGAGAG CCGGCACTCT CAGTTGCCCT
451  CTGGTTGAGT TGGGGGGCAG CTCTGGGGGC CGTGGCTTGT GCCATGGCTC
501  TGCTGACCCA ACAAACAGAG CTGCAGAGCC TCAGGAGAGA GGTGAGCCGG
551  CTGCAGGGGA CAGGAGGCC CTCCCAGAAT GGGGAAGGGT ATCCCTGGCA
601  GAGTCTCCCG GAGCAGAGTT CCGATGCCCT GGAAGCCTGG GAGAGTGGGG
651  AGAGATCCCG GAAAAGGAGA GCAGTGCTCA CCCAAAAACA GAAGAAGCAG
701  CACTCTGTCC TGCACCTGGT TCCCATTAA CACACCTCCA AGGATGACTC
751  CGATGTGACA GAGGTGATGT GGCAACCAGC TCTTAGGCGT GGGAGAGGCC
801  TACAGGCCCA AGGATATGGT GTCCGAATCC AGGATGCTGG AGTTTATCTG
851  CTGTATAGCC AGGTCCTGTT TCAAGACGTG ACTTTCACCA TGGGTCAGGT
901  GGTGTCTCGA GAAGGCCAAG GAAGGCAGGA GACTCTATTC CGATGTATAA
951  GAAGTATGCC CTCCCACCCG GACCGGGCCT ACAACAGCTG CTATAGCGCA
1001 GGTGTCTTCC ATTTACACCA AGGGGATATT CTGAGTGTCA TAATTCCCCG
1051 GGCAAGGGCG AAACCTTAACC TCTCTCCACA TGGAACCTTC CTGGGGTTTG
1101 TGAAACTGTG ATTGTGTTAT AAAAAGTGGC TCCCAGCTTG GAAGACCAGG
1151 GTGGGTACAT ACTGGAGACA GCCAAGAGCT GAGTATATAA AGGAGAGGGA
1201 ATGTGCAGGA ACAGAGGCGT CTTCCTGGGT TTGGCTCCCC GTTCCTCACT
1251 TTTCCCTTTT CATTCCCACC CCCTAGACTT TGATTTTACG GATATCTTGC
1301 TTCTGTTCCC CATGGAGCTC CGAATTCTTG CGTGTGTGTA GATGAGGGGC
1351 GGGGGACGGG CGCCAGGCAT TGTTACAGAC TGGTCGGGGC CCACTGGAAG
1401 CATCCAGAAC AGCACCACCA TCTAACGGCC GCTCGAGGGA AGCACCCGGC
1451 GGTTTGGGCG AAGTC
```

The proposed transmembrane domains are boxed

human G70 protein sequence (SEQ ID NO 2)

```

  1  MPASSPFLLA PKGPPGNMGG PVREPALSVA LWLSWGAALG AVACAMALLT
 51  QQTELQSLRR EVSRLQGTGG PSQNGEGYPW QSLPEQSSDA LEAWESGERS
101  RKRRAVLTQK QKKQHSLVHL VPINATSKDD SDVTEVMWQP ALRRGRGLQA
151  QGYGVRIQDA GYVLLYSQVL FQDVTFTMGQ VVSREGQGRQ ETLFRCIRSM
201  PSHPDRAVNS CYSAGVFHLH QGDILSVIIP RARAKLNLSP HGTFGLGFV
```

FIG. 2A

Sequence of mouse G70 (SEQ ID NOS: 3 and 4)

Mouse G70 (SEQ ID NO 3)

1	CATGCCGAGT	GCTTTGTGTG	TGTTACCTGC	TCTAAGAAGC	TGGCTGGGCA
51	GCGTTTCACC	GCTGTGGAGG	ACCAGTATTA	CTGCGTGGAT	TGCTACAAGA
101	ACTTTGTGGC	CAAGAAGTGT	GCTGGATGCA	AGAACCCCAT	CACTGGGTTT
151	GGTAAAGGCT	CCAGTGTGGT	GGCCTATGAA	GGACAATCCT	GGCACGACTA
201	CTGCTTCCAC	TGCAAAAAAT	GCTCCGTGAA	TCTGGCCAAC	AAGCGCTTTG
251	TATTTTCATAA	TGAGCAGGTG	TATTGCCCTG	ACTGTGCCAA	AAAGCTGTAA
301	CTTGACGGCT	GCCCTGTCCT	TCCTAGATAA	TGGCACCAAA	TTCTCCTGAG
351	GCTAGGGGGG	AAGGAGTGTC	AGAGTGTCAC	TAGCTCGACC	CTGGGGACAA
401	GGGGGACTAA	TAGTACCCTA	GCTTGATTTC	TTCCTATTCT	CAAGTTCCTT
451	TTTATTTCTC	CCTTGCGTAA	CCCGCTCTTC	CCTTCTGTGC	CTTTGCCTGT
501	ATTCCCACCC	TCCCTGCTAC	CTCTTGGCCA	CCTCACTTCT	GAGACCACAG
551	CTGTTGGCAG	GGTCCCTAGC	TCATGCCAGC	CTCATCTCCA	GGCCACATGG
601	GGGGCTCAGT	CAGAGAGCCA	GCCCTTTCGG	TTGCTCTTTG	GTTGAGTTGG
651	GGGGCAGTTC	TGGGGGCTGT	GACTTGTGCT	GTCGCACTAC	TGATCCAACA
701	GACAGAGCTG	CAAAGCCTAA	GGCGGGAGGT	GAGCCGGCTG	CAGCGGAGTG
751	GAGGGCCTTC	CCAGAAGCAG	GGAGAGCGCC	CATGGCAGAG	CCTCTGGGAG
801	CAGAGTCCTG	ATGTCCTGGA	AGCCTGGAAG	GATGGGGCGA	AATCTCGGAG
851	AAGGAGAGCA	GTA ¹ CTACCC	AGAAGCACAA	GAAGAAGCAC	TCAGTCCTGC
901	ATCTTGTTCC	AGTTAACATT	ACCTCCAAGG	ACTCTGACGT	GACAGAGGTG
951	ATGTGGCAAC	CAGTACTTAG	GCGTGGGAGA	GGCCTGGAGG	CCCAGGGAGA
1001	CATTGTACGA	GTCTGGGACA	CTGGAATTTA	TCTGCTCTAT	AGTCAGGTCC
1051	TGTTTCATGA	TGTGACTTTC	ACAATGGGTC	AGGTGGTATC	TCGGGAAGGA
1101	CAAGGGAGAA	GAGAAACTCT	ATTCCGATGT	ATCAGAAGTA	TGCCTTCTGA
1151	TCCTGACCGT	GCCTACAATA	GCTGCTACAG	TGCAGGTGTC	TTTCATTTAC
1201	ATCAAGGGGA	TATTATCACT	GTCAAAATTC	CACGGGCAAA	CGCAAAACTT
1251	AGCCTTTCTC	CGCATGGAAC	ATTCTGGGG	TTTGTGAAAC	TATGATTGTT
1301	ATAAAGGGGG	TGGGGATTTC	CCATTCCAAA	AACTGGCTAG	ACAAAGGACA
1351	AGGAACGGTC	AAGAACAGCT	CTCCATGGCT	TTGCCTTGAC	TGTTGTTCTT
1401	CCCTTTGCCT	TTCCCGCTCC	CACTATCTGG	CCTTTGACTC	CATGGATATT
1451	AAAAAAGTAG	AATATTTTGT	GTTTATCTCC	CAAAAA	

FIG. 2B

Mouse G70 Length: 241 (SEQ ID NO 4)

```
1  MPASSPGHMG GSVREPALSV ALWLSWGAVL GAVTCAVALL IQQTELQSLR
51 REVSRLQRSG GPSQKQGERP WQSLWEQSPD VLEAWKDGAK SRRRRAVLTQ
101 KHKKKHSLVH LVPVNITSKD SDVTEVMWQP VLRRGRGLEA QGDIVRVWDT
151 GIYLLYSQVL FHDVTFTMGQ VVSREGQGRR ETLFRCIRSM PSDPDRAVNS
201 CYSAGVFHLH QGDIITVKIP RANAKLSLSP HGTFLGFVKL *
```

G-70 FLAG des92 (smuG70) Strain #4081 (SEQ ID NO 19):

```
MDYKDDDDKKHKKKHSVLHLVPVNITSKDSDVTEVMWQPVLRRGRGLEAQGDIVRVWDTGIY
LLYSQVLFHDVTFTMGQVVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDII
TVKIPRANAKLSLSPHGTFLGFVKL*
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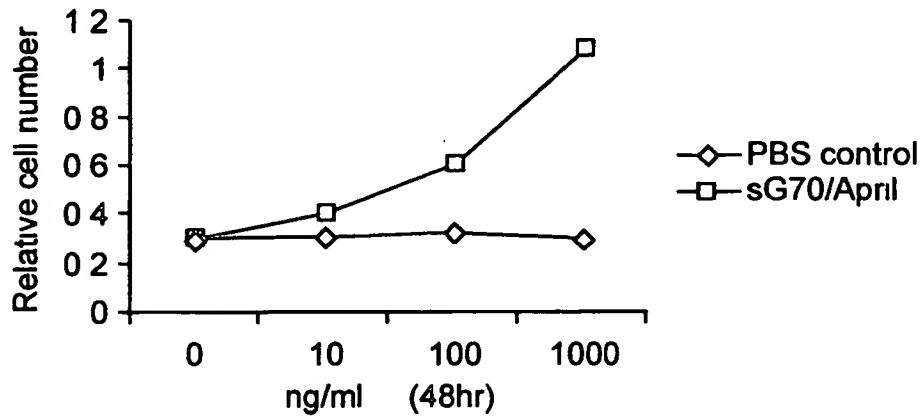
FIG. 3

Alignm of human and mouse G70

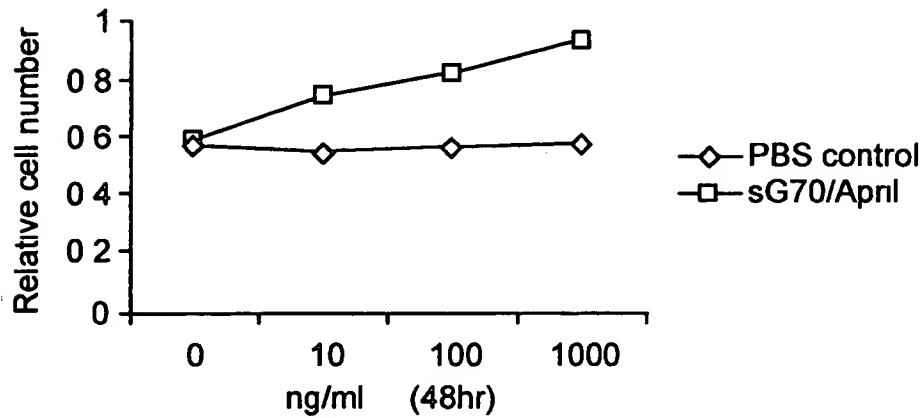
mouse:	1	MPASS-----PGHMGGS	VREPALSVALWLSWGAVLGAVTCAVALL	IQQTELQSLRR	51
		MPASS	PG+MGG	VREPALSVALWLSWGA LGAV CA+ALL	QQTELQSLRR
human:	1	MPASSPFLAPKGP	PGNMGGP	VREPALSVALWLSWGAALGAVACAMALL	TQQTELQSLRR
					60
mouse:	52	EVSRLQ	SGGPSQKQGERPWQSLWEQSPDVLEAWKDGAKSRRRRRAVLTQKHKKKHSVLHL		111
		EVSRLQ	+GGPSQ	PWQSL EQS D LEAW+ G +SR+RRAVLTQK KK+HSVLHL	
human:	61	EVSRLQ	GTGGPSQNGEGYPWQSLPEQSSDALEAWESGERSRKRRAVLTQKQKKQHSVLHL		120
mouse:	112	VPVNIT	SKD-SDVTEVMWQPVLRGRGRGLEAQGDIVRVWDTGIYLLYSQVLFHDVFTTMGQ		170
		VP+N	TSKD SDVTEVMWQPVLRGRGL+AQG VR+ D G+YLLYSQVLF DVTFTMGQ		
human:	121	VPINAT	SKDDSDVTEVMWQPVLRGRGRGLQQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQ		180
mouse:	171	VVSREG	QRRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDIITVKIPRANAKLSLSP		230
		VVSREG	QGR+ETLFR	CIRSMPS PDRAYNSCYSAGVFHLHQGDI+V IPRA AKL+LSP	
human:	181	VVSREG	QGRQETLFR	CIRSMPSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNLSP	240
mouse:	231	HGTF	FLGFVKL	240	
		HGTF	FLGFVKL		
human:	241	HGTF	FLGFVKL	250	

FIG. 4A

Effect of sG70/April on Raji cell proliferation



Effect of sG70/April on Jurkat cell proliferation



Effect of sG70/April on K562 cell proliferation

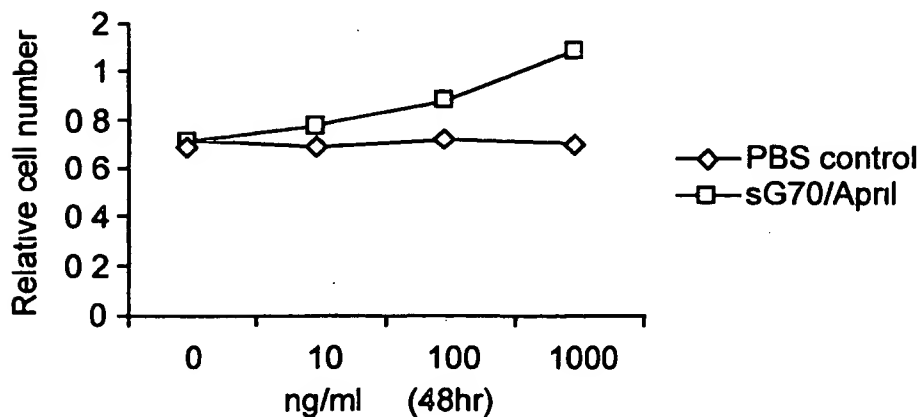
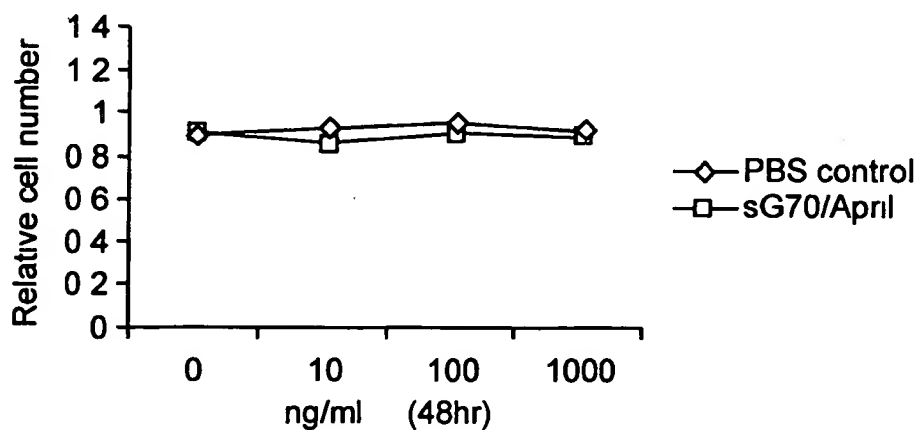
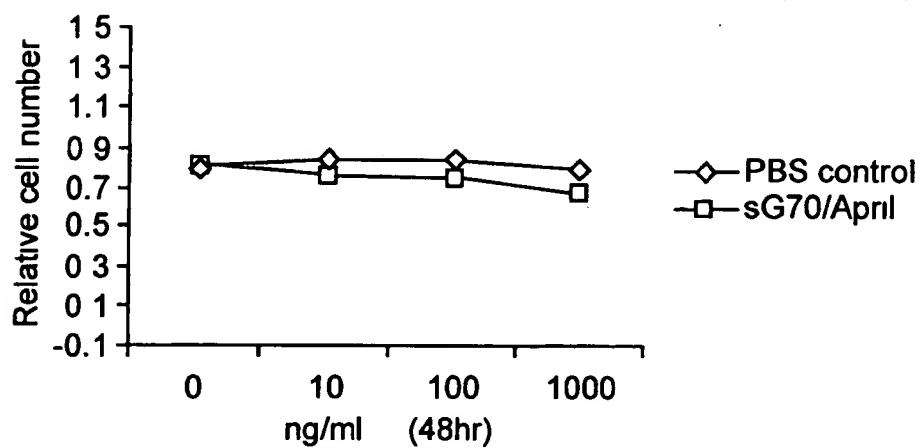


FIG. 4B

Effect of sG70/April on U937 cell proliferation



Effect of sG70/April on 293 T cell proliferation



Effect of sG70/April on 3T3 cell proliferation

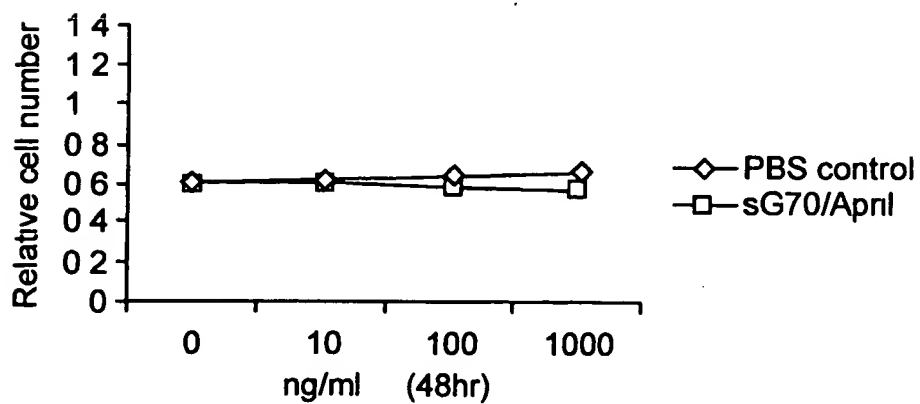


FIG. 5A

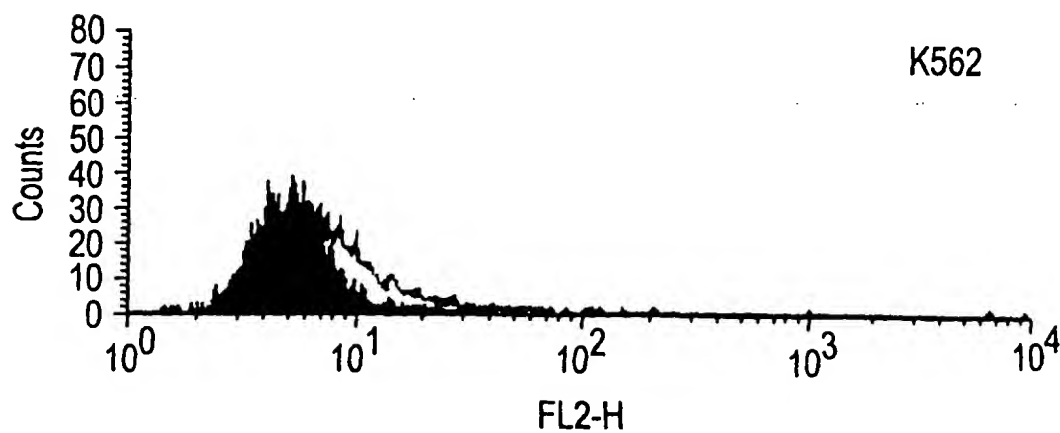
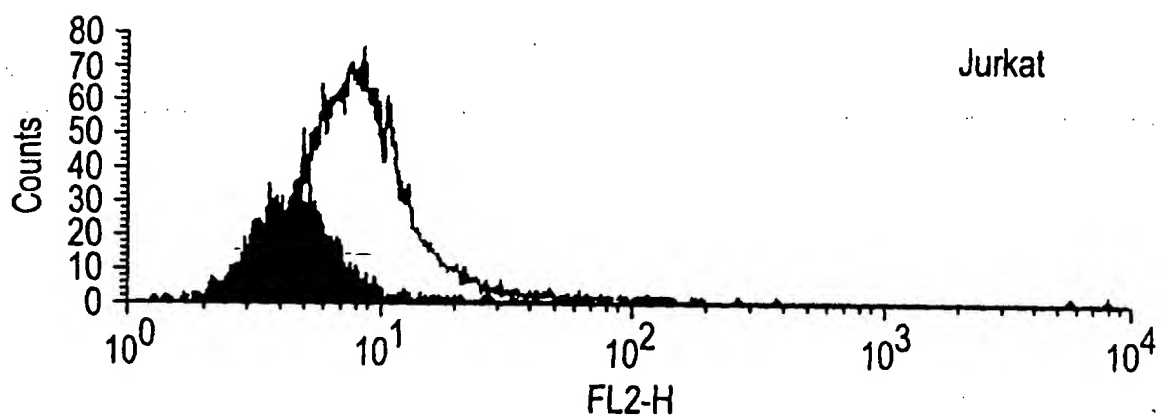
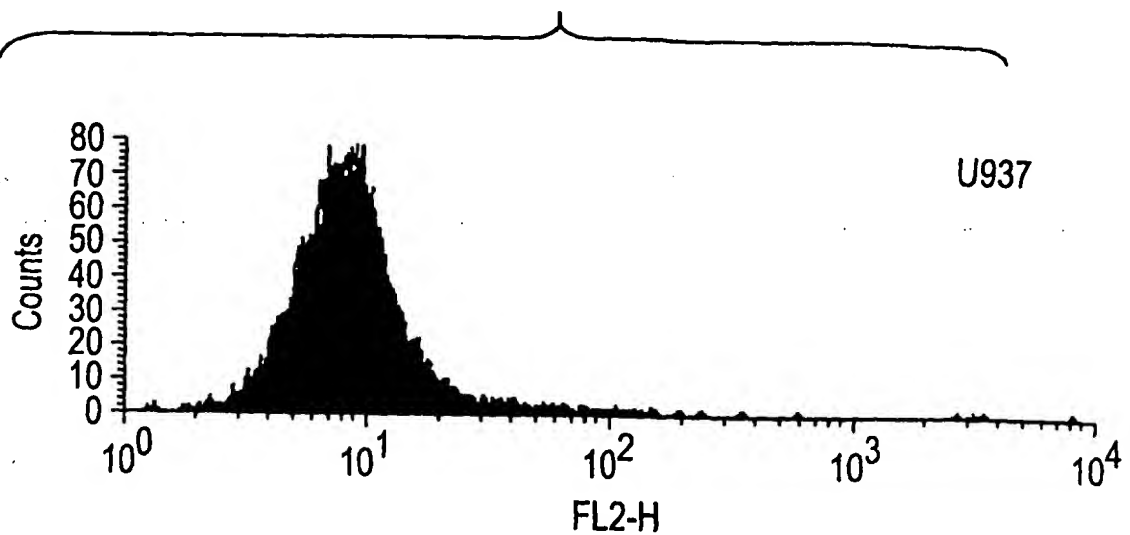


FIG. 5B-1

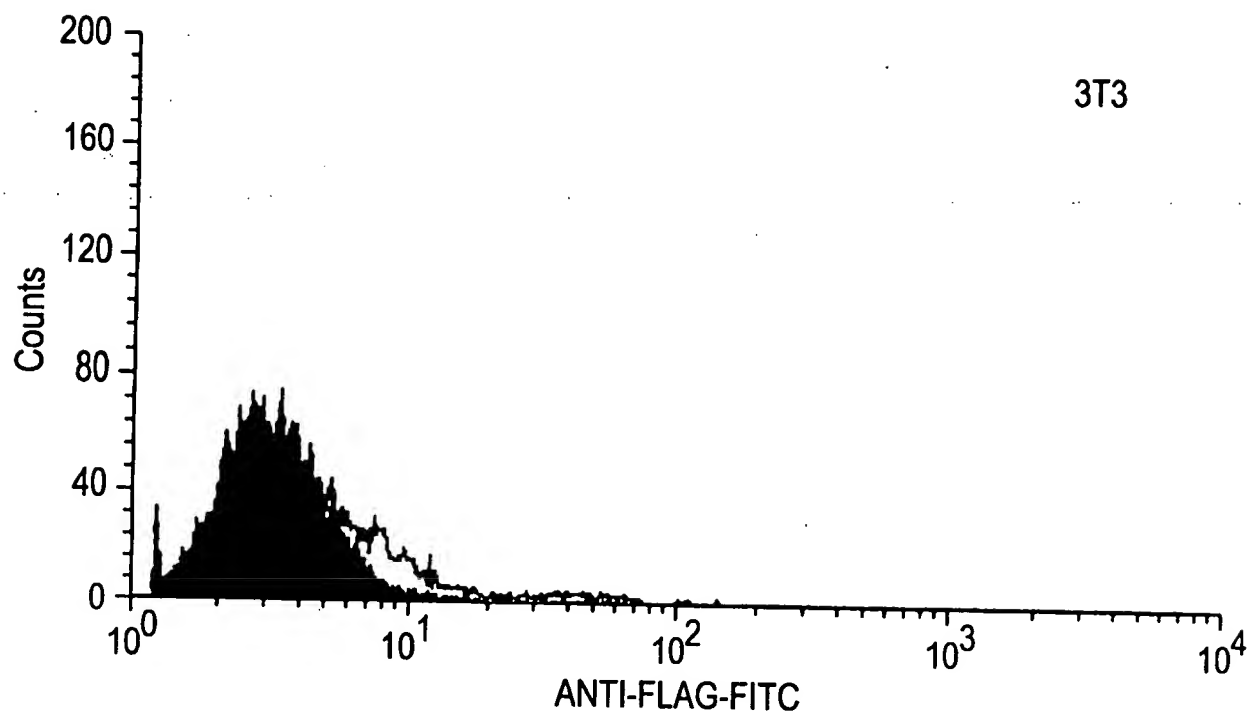


FIG. 5B-2

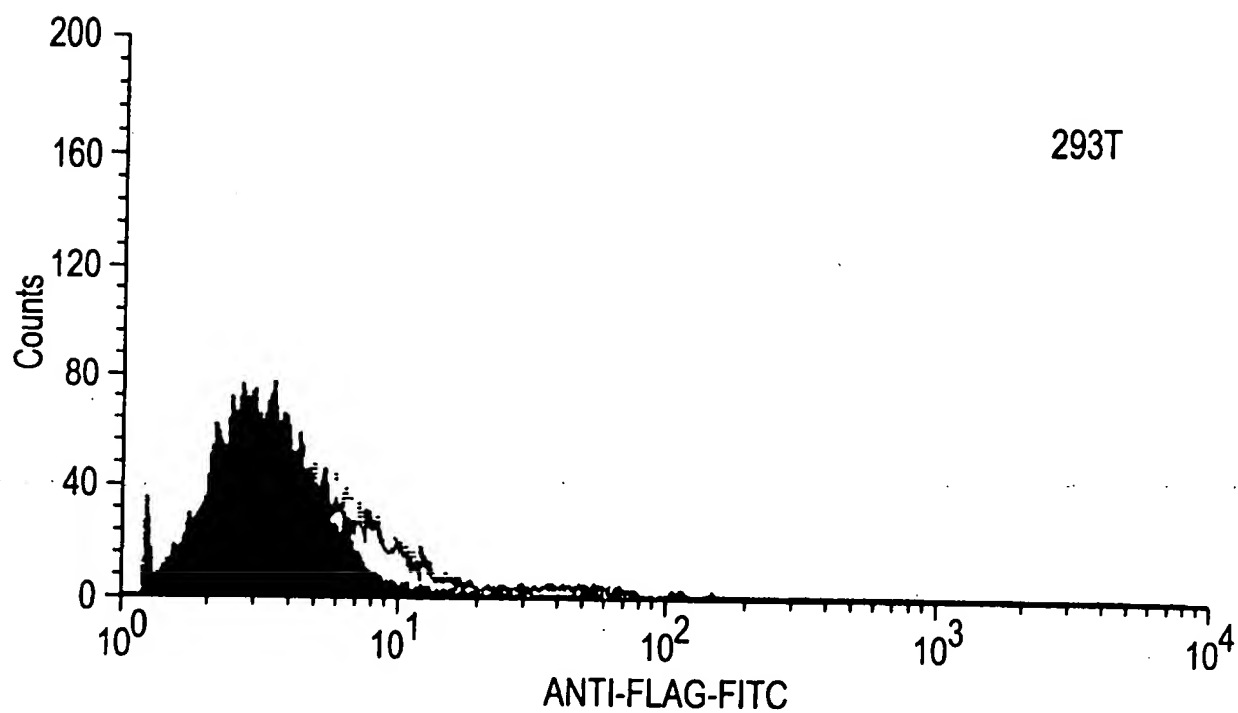


FIG. 5B-3

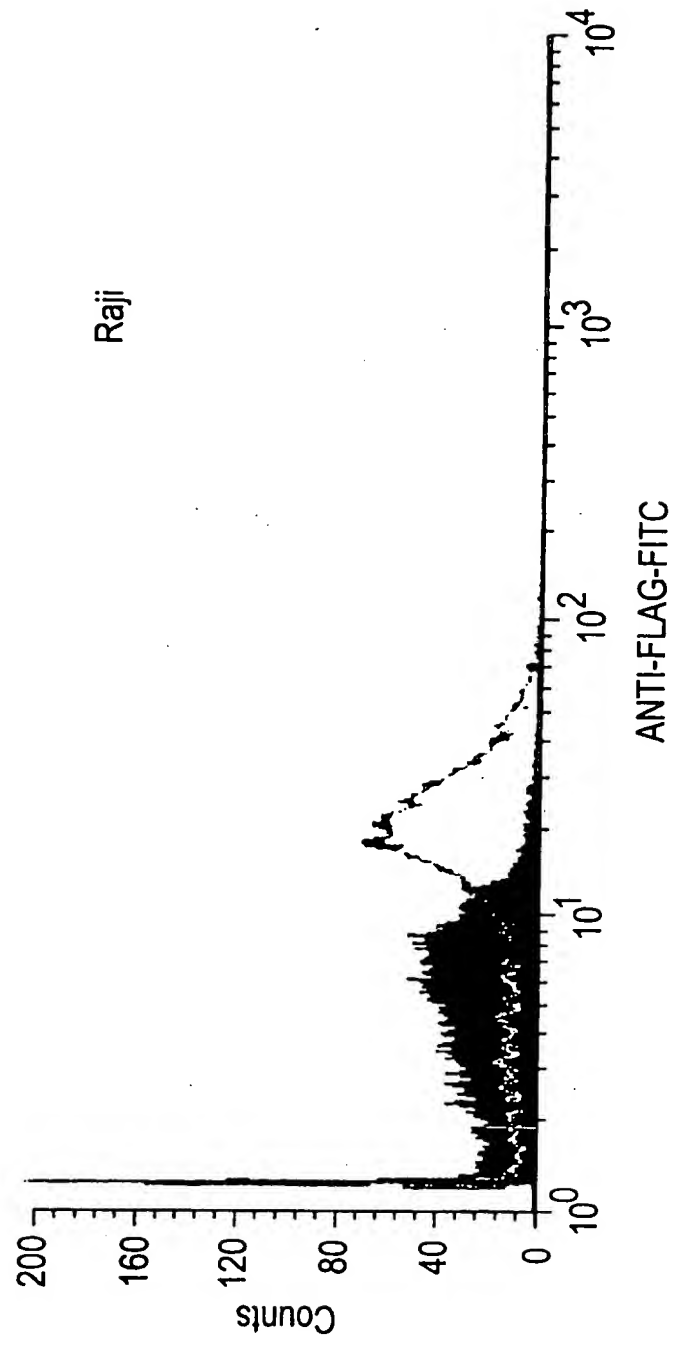
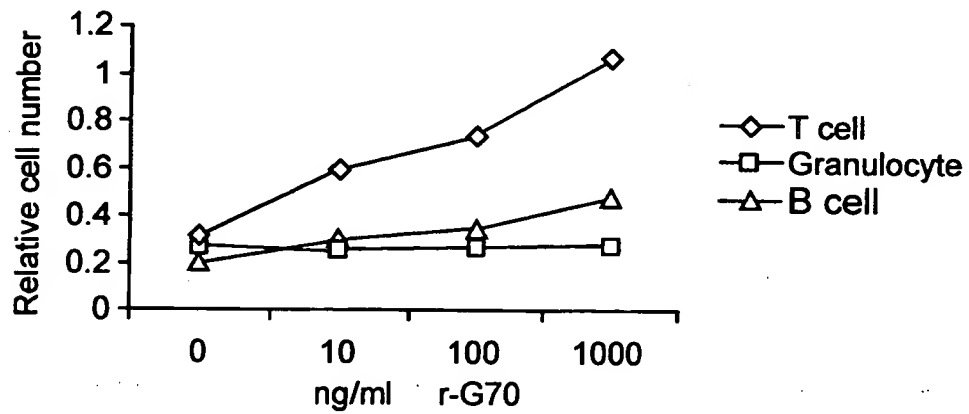


FIG. 6

The effect of r-G70/April on human peripheral blood B cell, T cell and Granulocyte



The effect of IL-2 and G70/April on human peripheral T cell proliferation

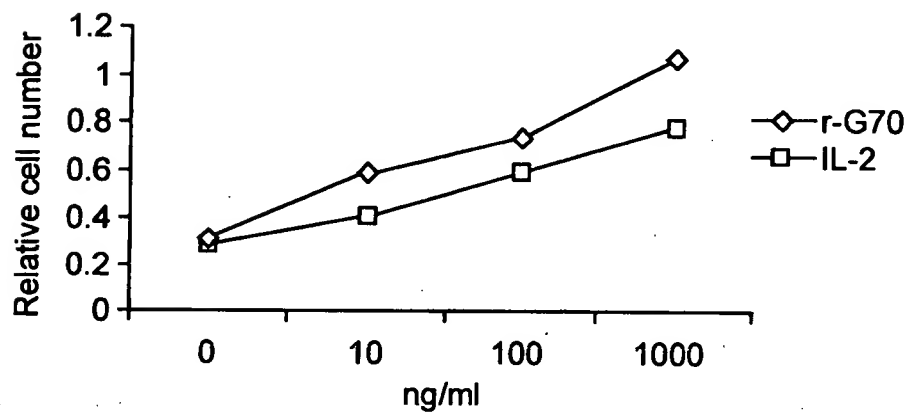
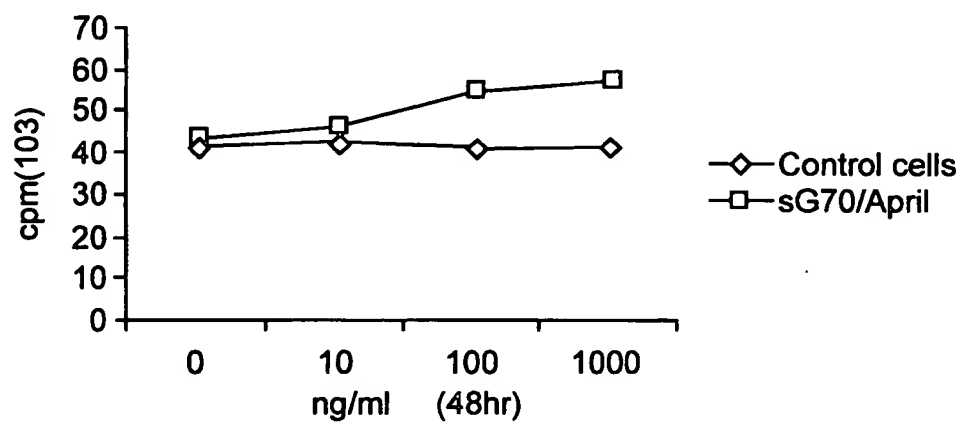


FIG. 7

Effect of sG70/April on murine B cell proliferation



Effect of sG70/April on murine T cell proliferation

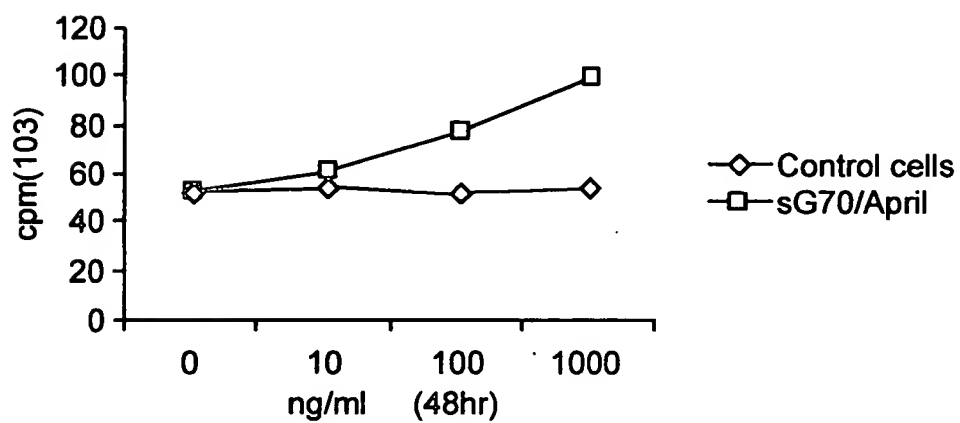


FIG. 8

Effect of G70/April on murine T cell
proliferation costimulated through CD28
antibody

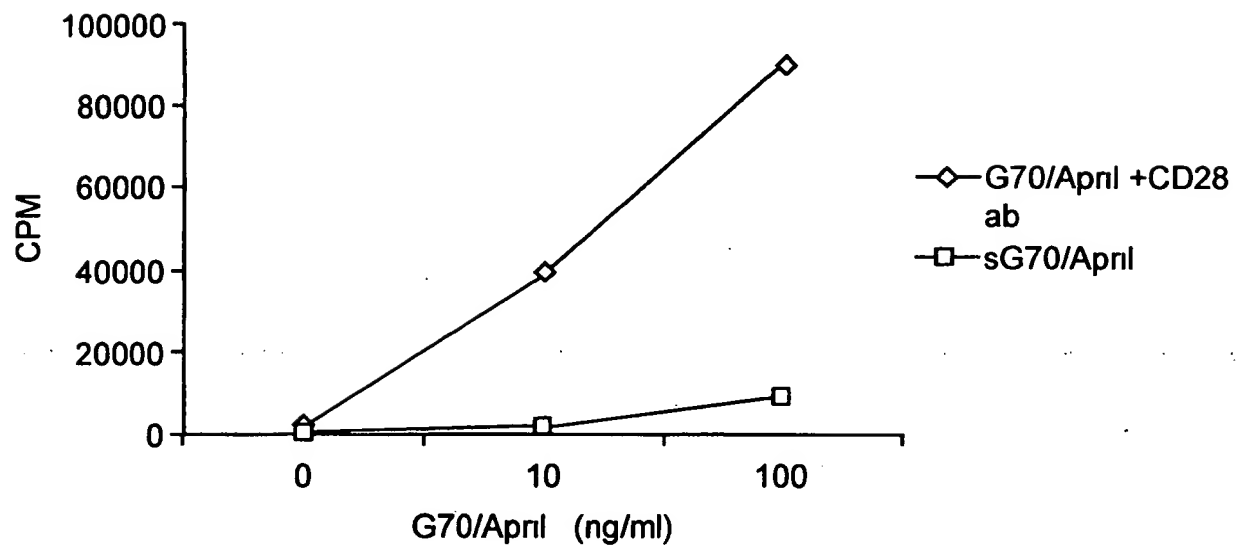


FIG. 9

Co-stimulatory activity of G70/April on mouse T cells

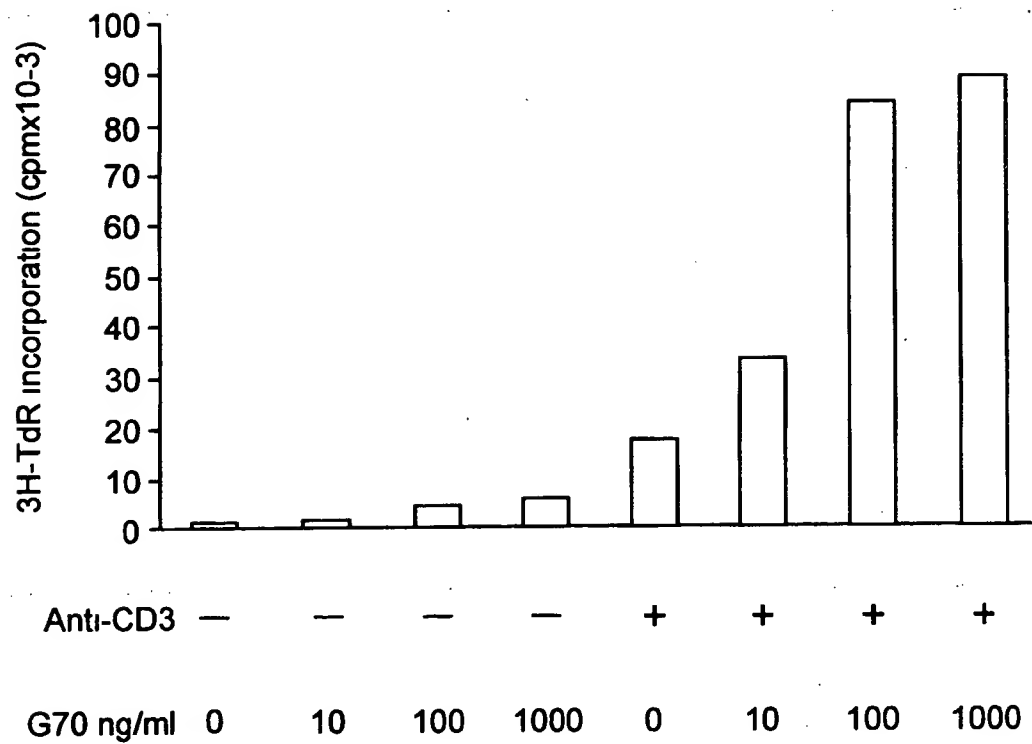


FIG. 10A

Human BCMA

Human (SEQ ID NO: 5):

1 MAGQCSQNEY FDSLLHACIP CQLRCSSNTP PLTCQRYCNA SVTNSVKGTN
51 AILWTCLGLS LIISLAVFVL MFLLRKISSE PLKDEFKNTG SGLLGMANID
101 LEKSRTGDEI ILPRGLE YTV EECTCEDCIK SKPKVDS DHC FPLPAMEEGA
151 TILVTTKTND YCKSLPAALS ATEIEKSISA R

Human (SEQ ID NO: 5):

MAGQCSQ **NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY** CNASVTNSVK
GTNA ILWTCL GLSLIISLAV FVLMFLLRKI SSEPLKDEFK NTGSGLLGMA
NIDLEKSRTG DEIILPRGLE YTVEECTCED CIKSKPKVDS DHC FPLPAME
EGATILVTTK TNDYCKSLPA ALSATEIEKS ISAR

hBCMA's extracellular domain (SEQ ID NO: 6):

MAGQCSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY CNASVTNSVK
GTNA

hBCMA's cysteine-rich consensus region (SEQ ID NO: 7):

CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C

hBCMA's transmembrane region (SEQ ID NO: 8):

ILWTCL GLSLIISLAV FVLMF

FIG. 10B

huBCMA-Fc (SEQ ID NO 9)

MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAGGG
GGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCWVDVSHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKS
LSLSPGK*

muBCMA-Fc (SEQ ID NO 10)

MAQQCFHSEYFDSLLHACKPCHLRCSNPPATCQPYCDPSVTSSVKGSYTGGGGG
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCWVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLS
LSPGK*

FIG. 11

Alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence

murine BCMA amino acid sequence Length 185 (SEQ ID NO 11)

1 MAQQCFHSEY FDSLLHACKP CHLRCSNPPA TCQPYCDPSV TSSVKGTYTIV

51 LWIFLGLTLV LSLALFTISF LLRKMNPEAL KDEPQSPGQL DGSQAQDKAD

101 TELTRIRAGD DRIFPRSLEY TVEECTCEDC VKSKPKGSDS HFFPLPAMEE

151 GATILVTTKT GDYKSSVPT ALQSVMGMEK PTHTR

alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence

Query 4 MAGQCSQNEYFDSILLHACIPCQLRCSSTPPLTCQRYCNASVTNSVKGTNAILWTCGLGS 63
MA QC +EYFDSILLHAC PC LRCS+ PP TCQ YC+ SVT+SVKGT +LW LGL+

Sbjct 1 MAQQCFHSEYFDSILLHACKPCHLRCSN--PPATCQPYCDPSVTSSVKGTYTIVLWIFLGLT 58

Query 64 LIISLAVFVLMFLLRKISSEPLKDEFKNTG----SGLLGMANIDLEKSRTGDEIILPRGL 119
L++SLA+F + FLLRK++ E LKDE ++ G S L A+ +L + R GD+ I PR L

Sbjct 59 LVLSLALFTISFLLRKMNPEALKDEPQSPGQLDGSQAQDKADTELTRIRAGDDRIFFRSL 118

Query 120 EYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKS-LPAAL-SATEI 177
EYTVEECTCEDC+KSKPK DSDH FPLPAMEEGATILVTTKT DY KS +P AL S +

Sbjct 119 EYTVEECTCEDCVKSKPKGSDSDHFFPLPAMEEGATILVTTKTGDYKSSVPTALQSVMG 178

Query 178 EKSISAR 184
EK R

Sbjct 179 EKPTHTR 185

FIG. 12A

Human TACI

huTACI (SEQ ID NO 14)

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTSCMSC
51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC
101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
151 PGLKLSADQV ALVYSTLGLC LCAVLCCFLV AVACFLKKRG DPCSCQPRSR
201 PRQSPAKSSQ DHAMEAGSPV STSPEPVETC SFCFPECRAP TQESAVTPGT
251 PDPTCAGRWG CHTRTTVLQP CPHIPDSGLG IVCVPAQEGG PGA

MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTSCMSC
KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCASICGQHPKQC
AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
PGLKLSADQV ALVYST LGLC LCAVLCCFLV AVACFLKKRG DPCSCQPRSR
PRQSPAKSSQ DHAMEAGSPV STSPEPVETC SFCFPECRAP TQESAVTPGT
PDPTCAGRWG CHTRTTVLQP CPHIPDSGLG IVCVPAQEGG PGA

huTACI's extracellular domain (SEQ ID NO 15)

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTSCMSC
51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC
101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
151 PGLKLSADQV ALVYST

FIG. 12B

huTACI's cysteine-rich consensus region (SEQ ID NO: 16):

CPEEQYWDPLLGTCTMSCKTICNHQSQR TCAAF C and

CRKEQGKFYDHLRDCISCASICGQHPKQCAYFC

transmembrane region (SEQ ID NO: 17):

LGLCLCAVLCCFLVAVACFL

hTACI-Fc (SEQ ID NO: 18):

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCTMSC
51 KTICNHQSQR TCAAFCRSL S CRKEQGKFYD HLLRDCISCA SICGQHPKQC
101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
151 PGLKLSADQV ALVYSGGGGG DKTHTCPPCP APELLGGPSV FLFPPKPKDT
201 LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY
251 RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT
301 LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS
351 DGSFFLYSKL TVDKSRWQQG NVFSCSV MHE ALHNHYTQKS LSLSPGK*

FIG. 13

Alignment of cysteine rich extracellular regions of human TACI and human BCMA

```
34 CPEEQYWDPLLGTCTMSCKTICNHQS QRTCAAFCSRSLSCRKEQGKFYDHL 82
   |   | | | | |   |   |   |   |
  8 CSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGT NAI 55

      83 LRDCISCASI 92
         |   |   |
      56 LWTCLGLSLI 65
```

FIG. 14A

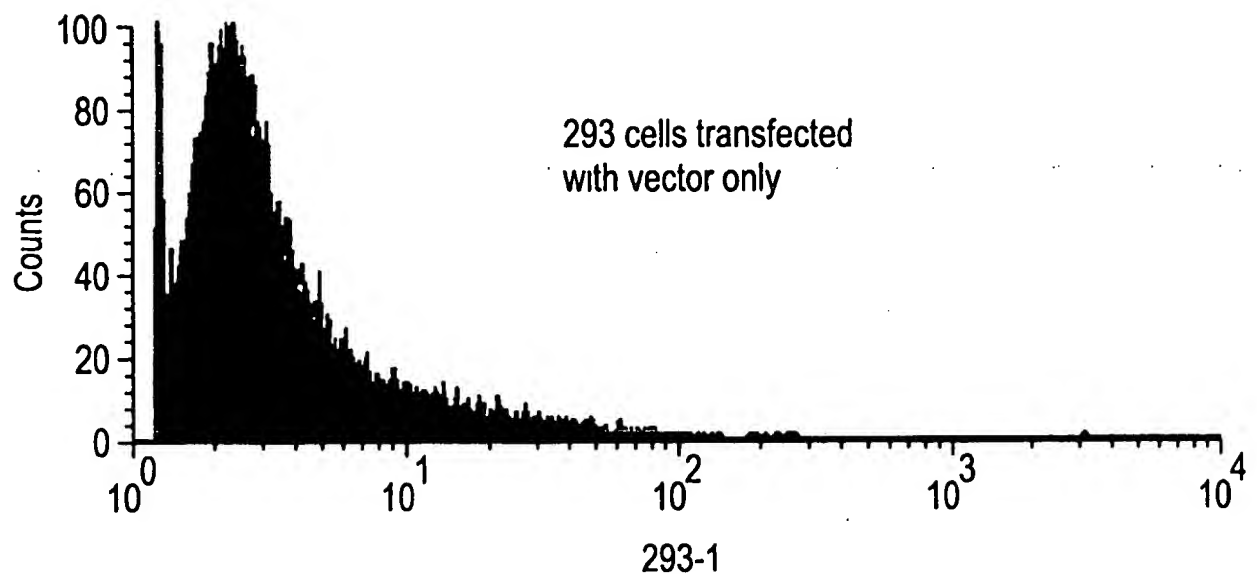


FIG. 14B

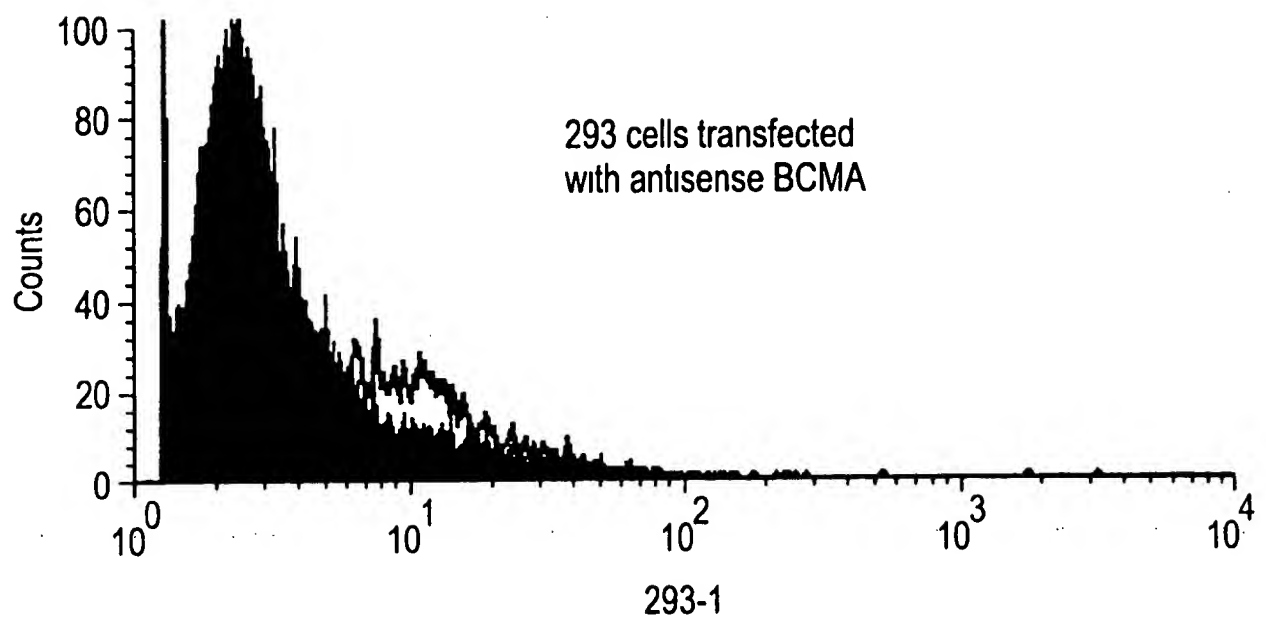


FIG. 14C

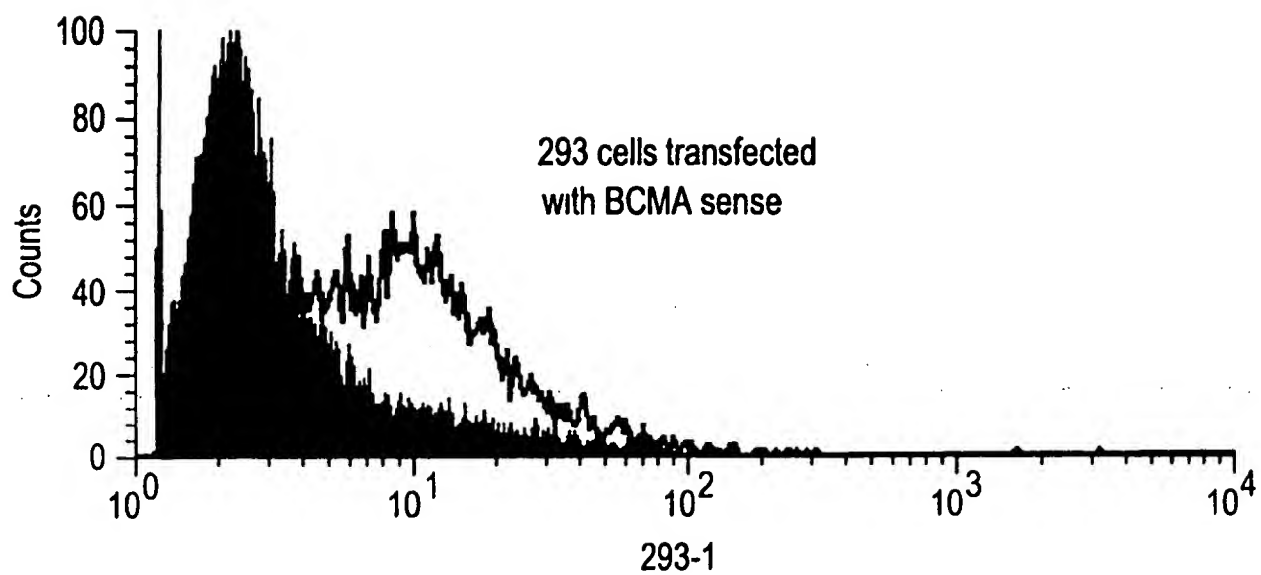


FIG. 15A

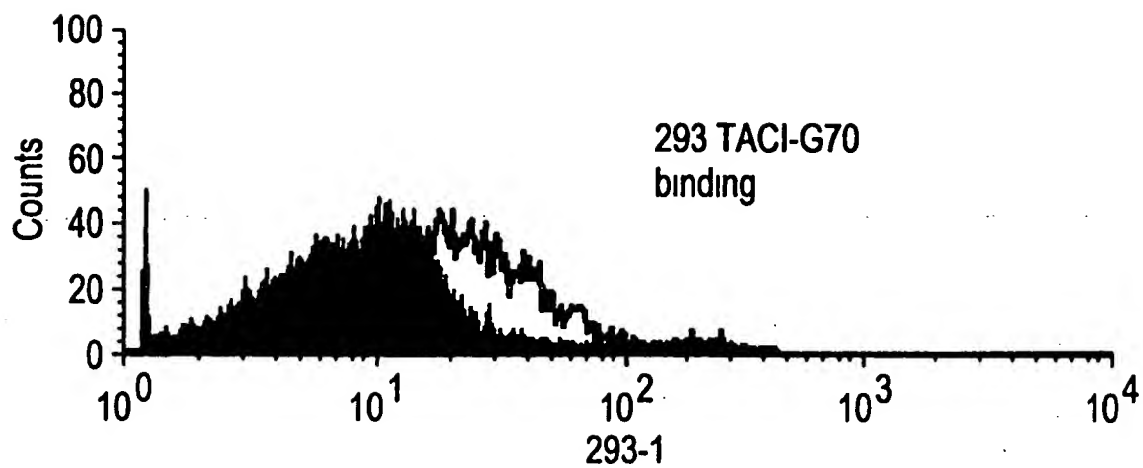


FIG. 15B

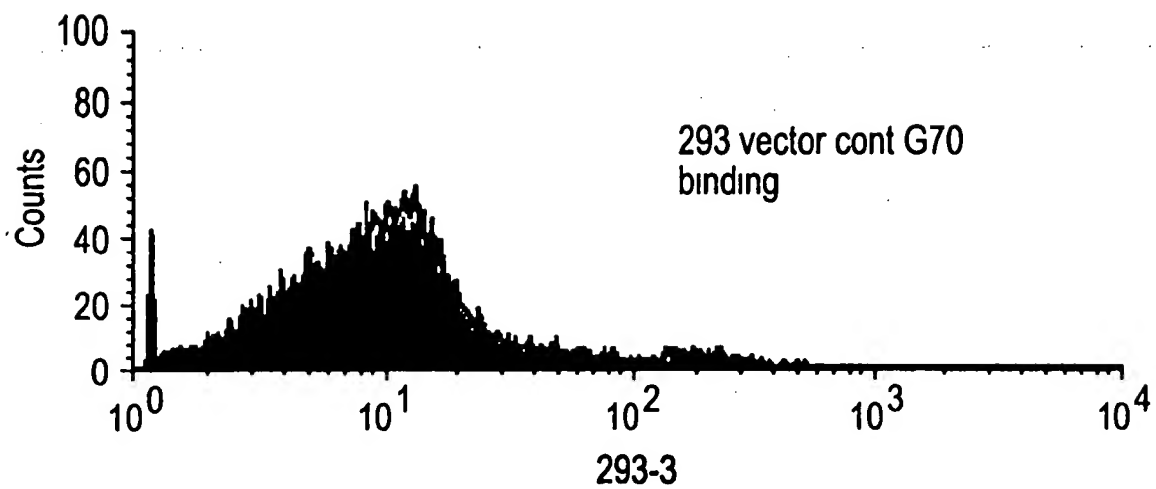


FIG. 16A

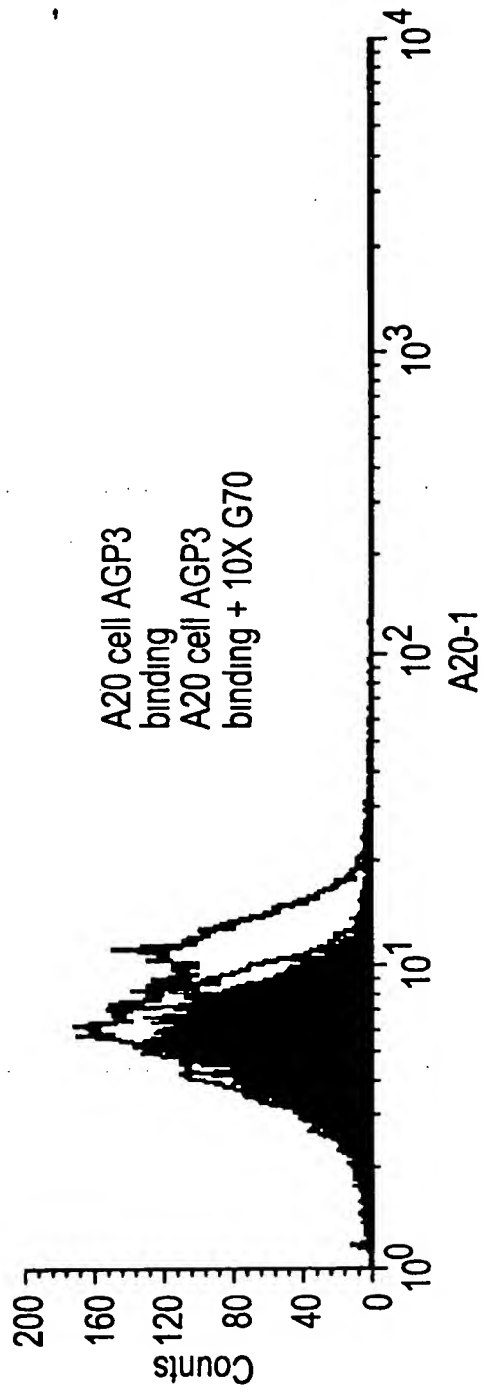


FIG. 16B

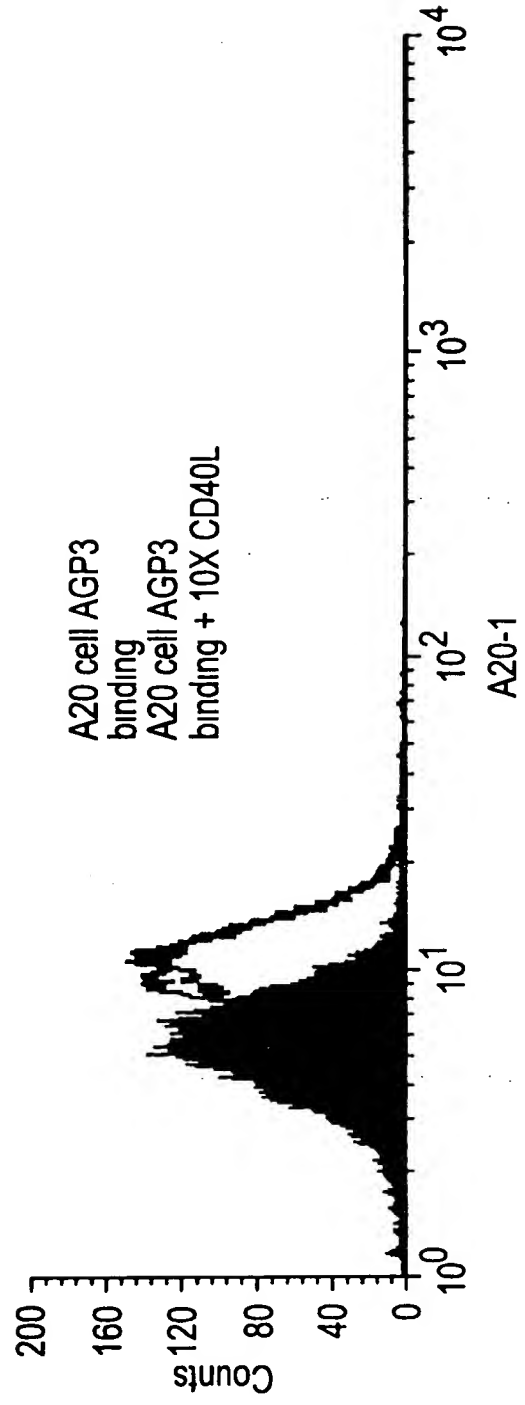


FIG. 16C

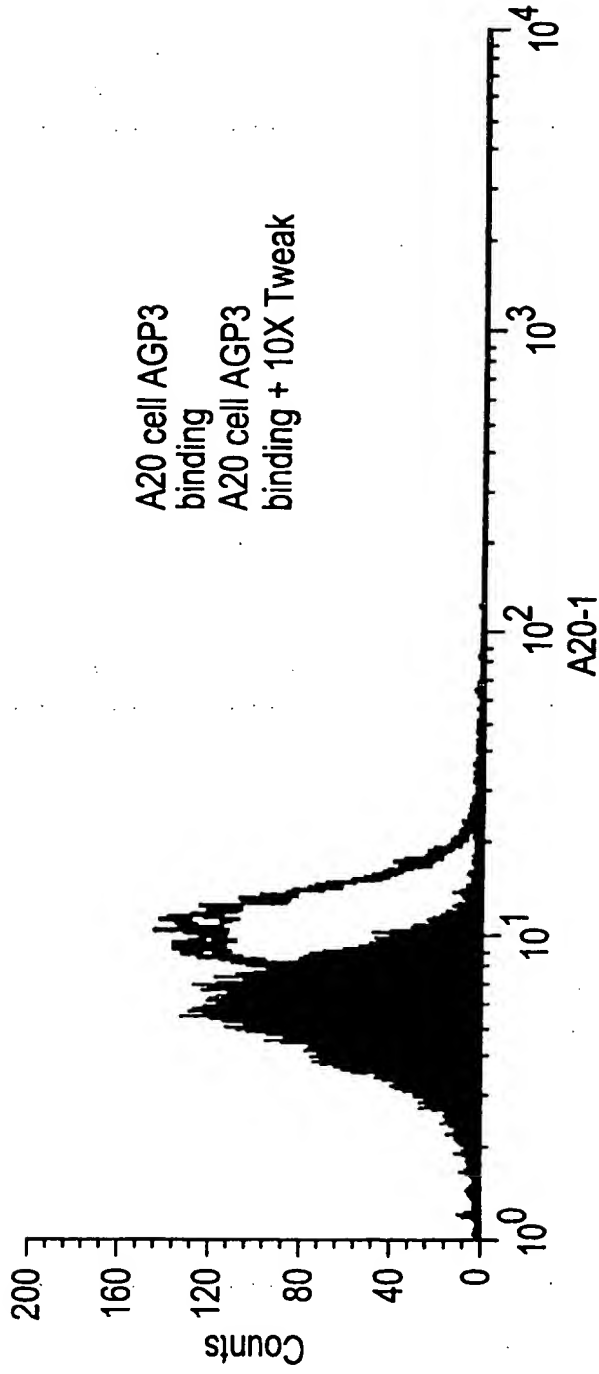


FIG. 16D

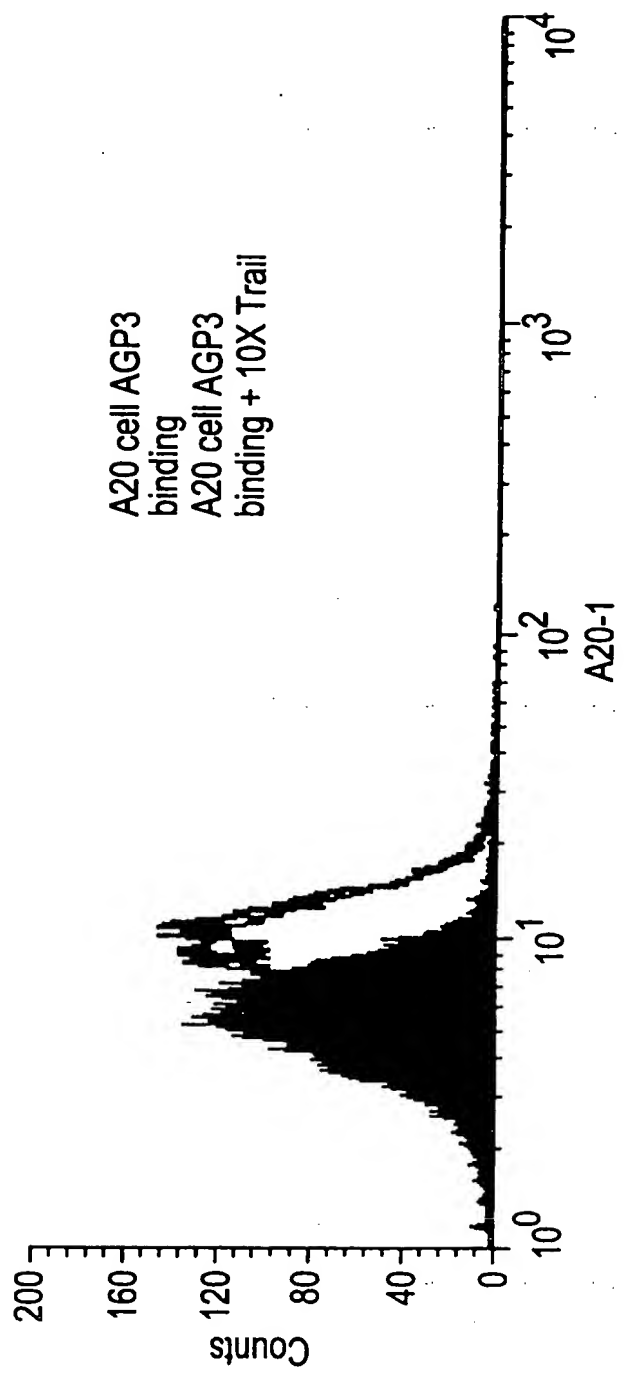


FIG. 17A

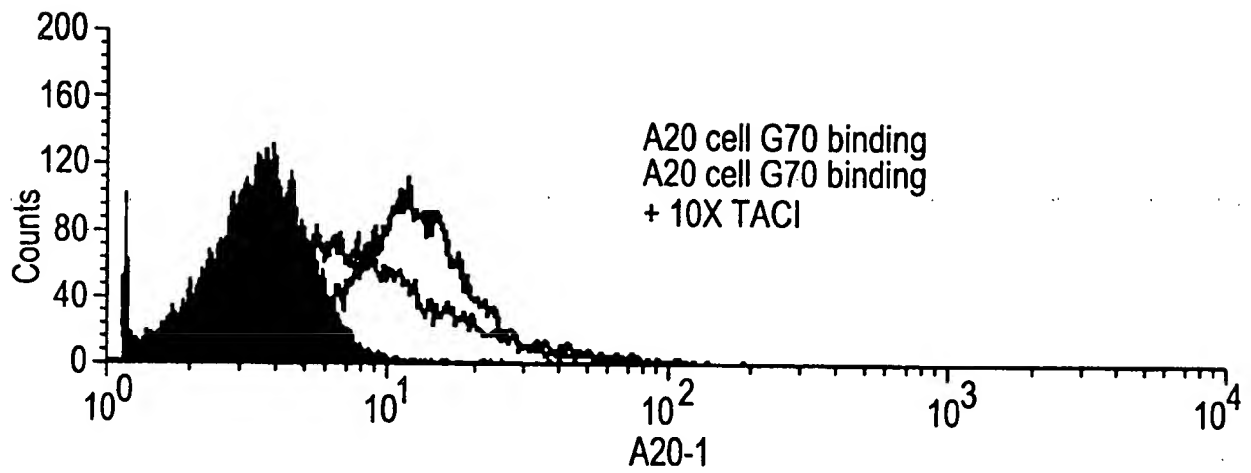


FIG. 17B

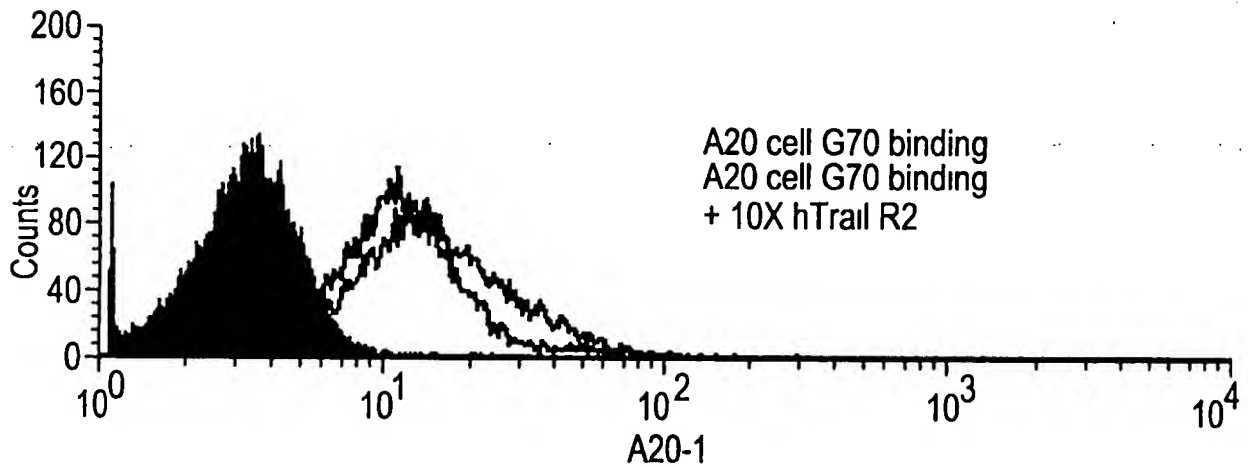


FIG. 17C

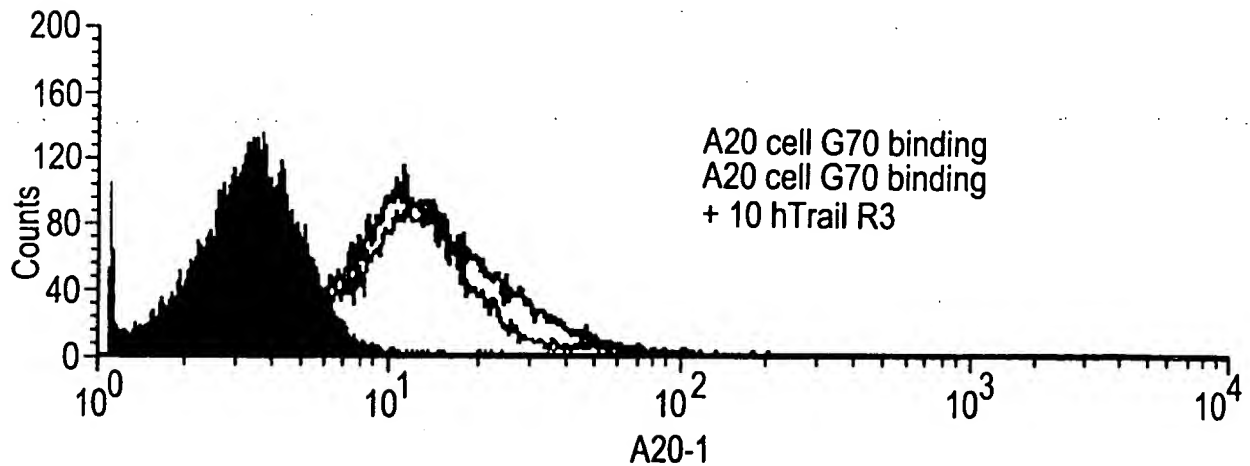


FIG. 18

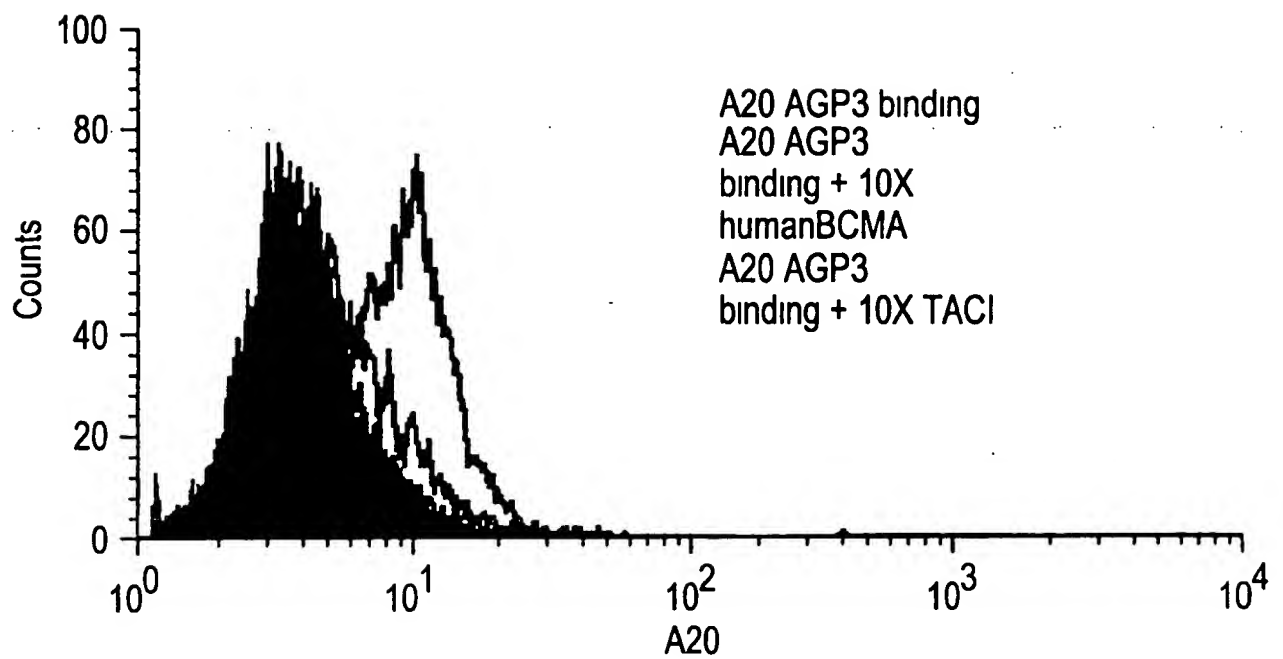


FIG. 19A

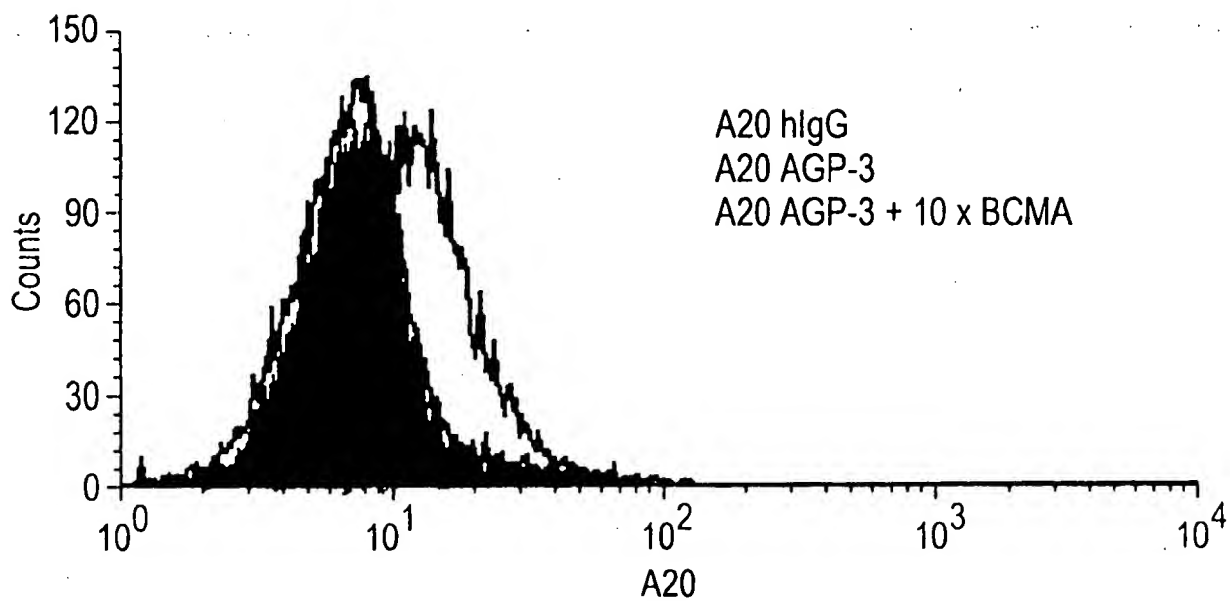


FIG. 19B

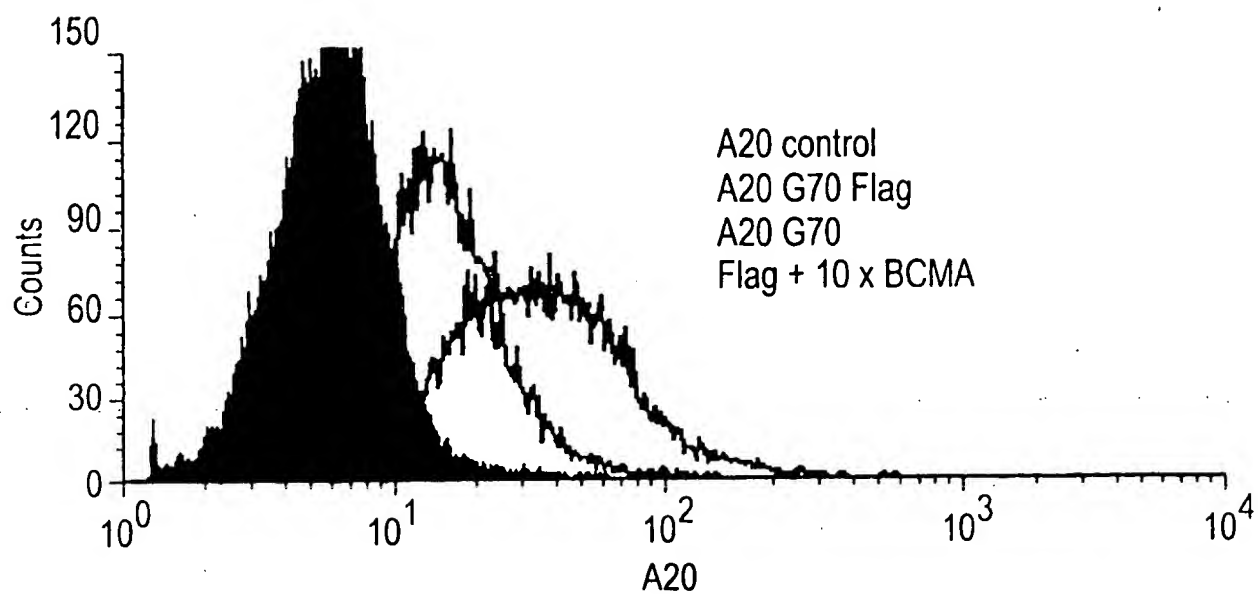


FIG. 20A

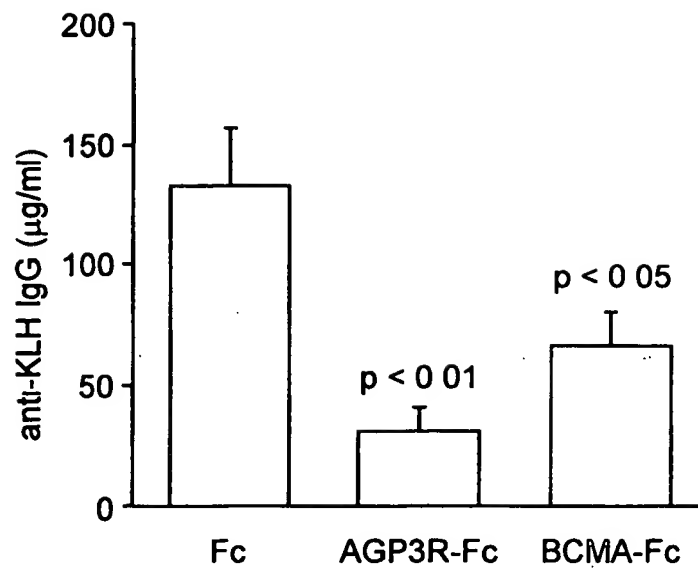


FIG. 20B

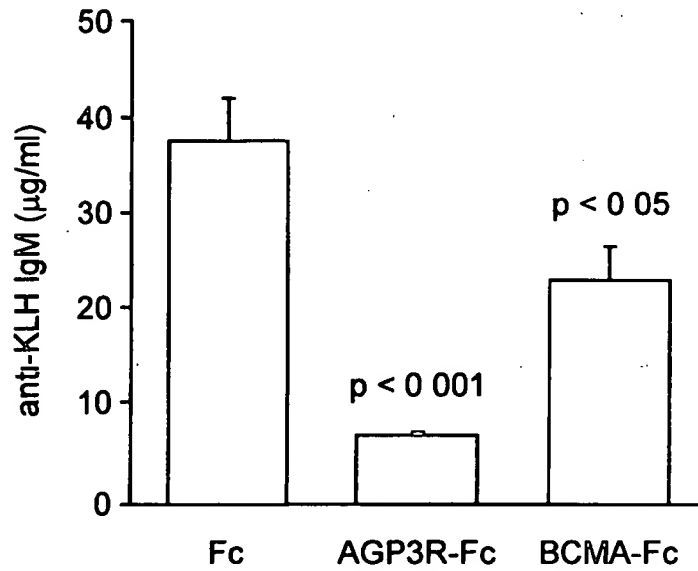


FIG. 20C

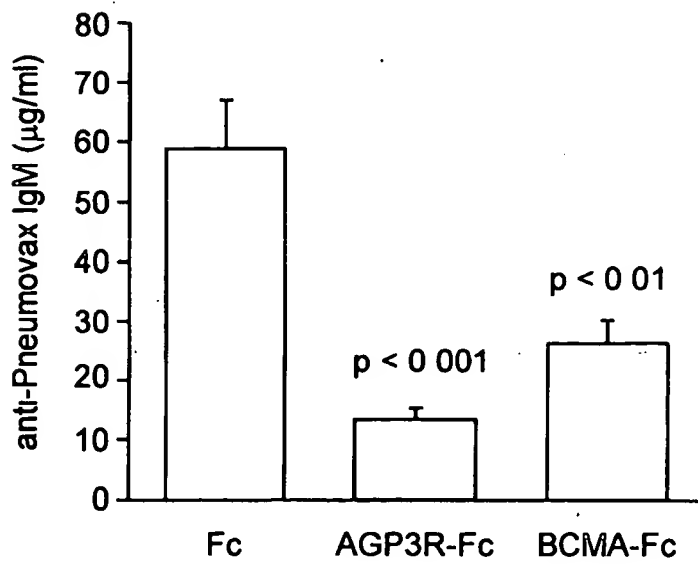


FIG. 21

Fc-humanAPRIL

Fc-humanAPRIL protein sequence including the signal sequence, Fc domain, linker (XhoI site) and APRIL

1	MEWSVFLFF	LSVTGVHSD	KHTCPPCPA	PELLGGPSVF
	LFPPKPKDTL			
51	MISRTPEVTC	VVVDVSHEDP	EVKFNWYVDG	VEVHNAKTKP
	REEQYNSTYR			
101	VVSVLTVLHQ	DWLNKEYKC	KVSNKALPAP	IEKTISKAKG
	QPREPQVYTL			
151	PPSRDELTKN	QVSLTCLVKG	FYPSDIAVEW	ESNGQPENNY
	KTTTPVLDSD			
201	GSFFLYSKLT	VDKSRWQQGN	VFSCVMHEA	LHNHYTQKSL
	SLSPGK SRAV			
251	LTQKQKKQHS	VLHLVPINAT	SKDDSDVTEV	MWQPALRRGR
	GLQAQGYGVR			
301	IQDAGVYLLY	SQVLFQDVTF	TMGQVVSREG	QGRQETLERC
	IRSMPSHPDR			
351	AYNSCYSAGV	FHLHQGDILS	VIIPRARAKL	NLSPHGTFGL
	FVKL*			

FIG. 22

Fc-HumanAPRIL and soluble human AGP3
stimulate proliferation of primary B cells

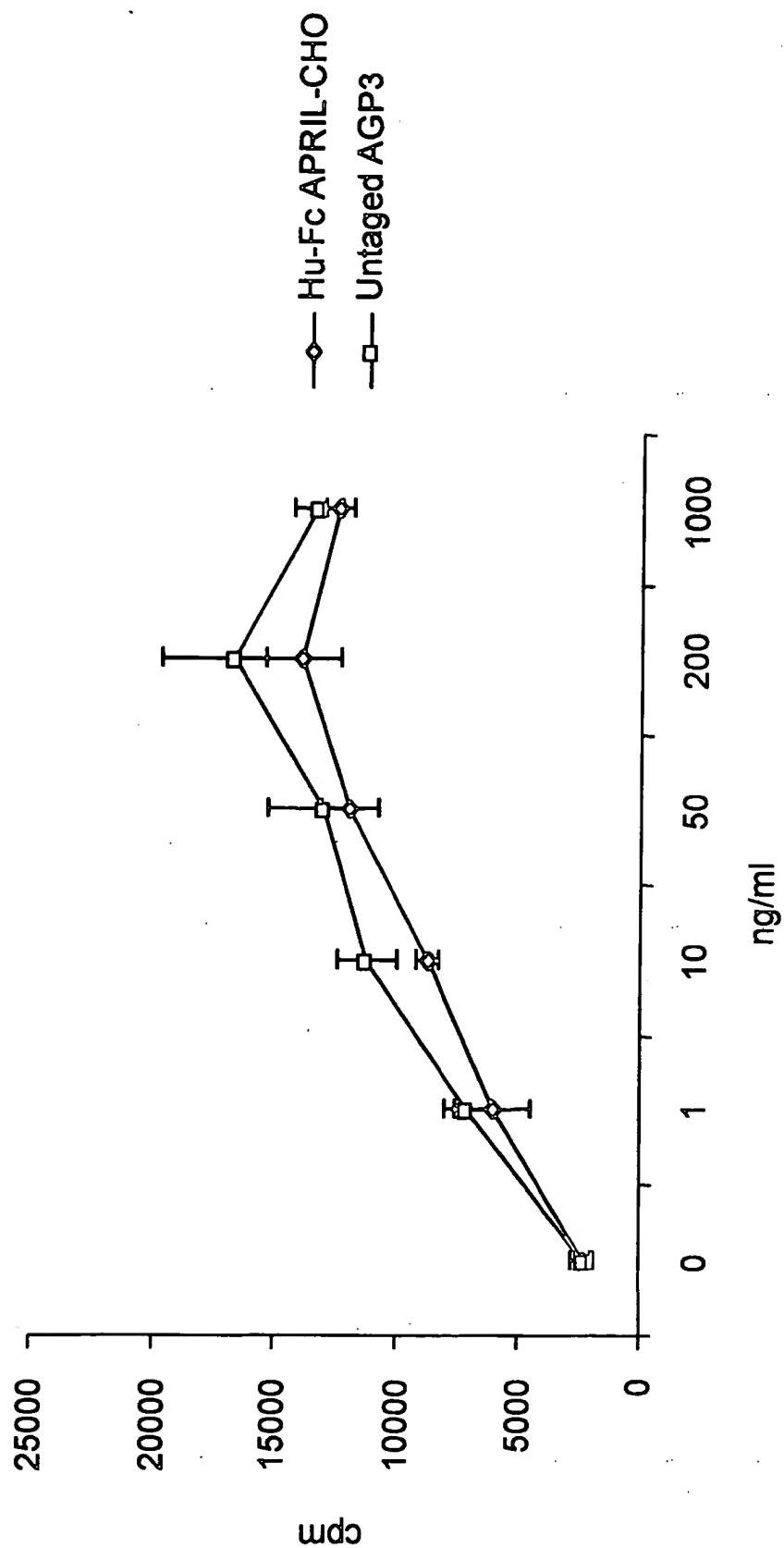


FIG. 23

hBCMA-Fc and wt hTACI-Fc inhibits
Flag-mAPRIL mediated mouse B cell
proliferation

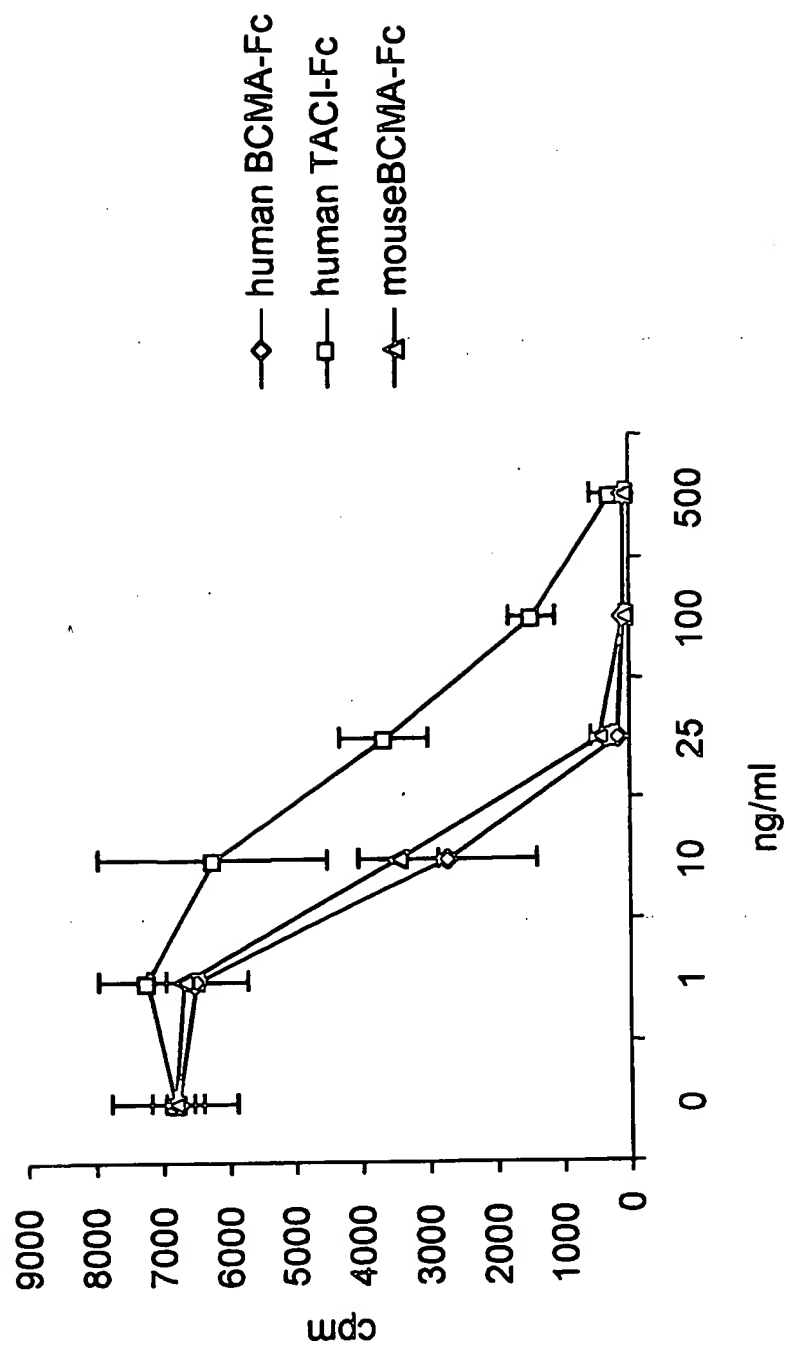


FIG. 24

hBCMA-Fc reduces PB B cell level *in vivo*
15 mg/kg ip on day 0, 3, and 6

BLOOD

WBC
10e6/ml

#Lym
10e6/ml

CD3+
#

CD3-B220+
#

BCMA-Fc
SD
t test

Fc
SD

Saline
SD

5 30 0 39 0 03318	3 81 0 43 0 01570	2 3 0 32 0 24737	1 3 0 27 0 00506
8 02 1 27	6 43 1 52	2 7 0 6	3 2 0 6
6 90 2 04	5 55 1 79	2 1 0 5	2 9 1 2

FIG. 25

hBCMA-Fc reduces spleen B cell levels *in vivo*
15 mg/kg ip on day 0, 3, and 6

Spleen	WBC 10e6/ml	Lym (%)	spleen lym# 10ml(x10e6)	CD3-B220+ (%)	CD3-B220+ #
BCMA-Fc SD t test	9.12 0.92 0.02778	97.9 0.51 0.89118	89.3 9.32 0.02668	45.5 1.29 0.00234	41.8 4.92 0.02088
FC SD	11.49 1.62	97.9 0.38	112.5 15.65	50.6 1.95	57.1 9.67
Saline SD	11.48 1.71	98.5 0.1	113.1 16.9	53.7 6.7	48.5 29.15

FIG. 26

Flag-mAPRIL and hAGP3 mediated IgA production
inhibited by hBCMA-Fc and hTACI-Fc *in vitro*

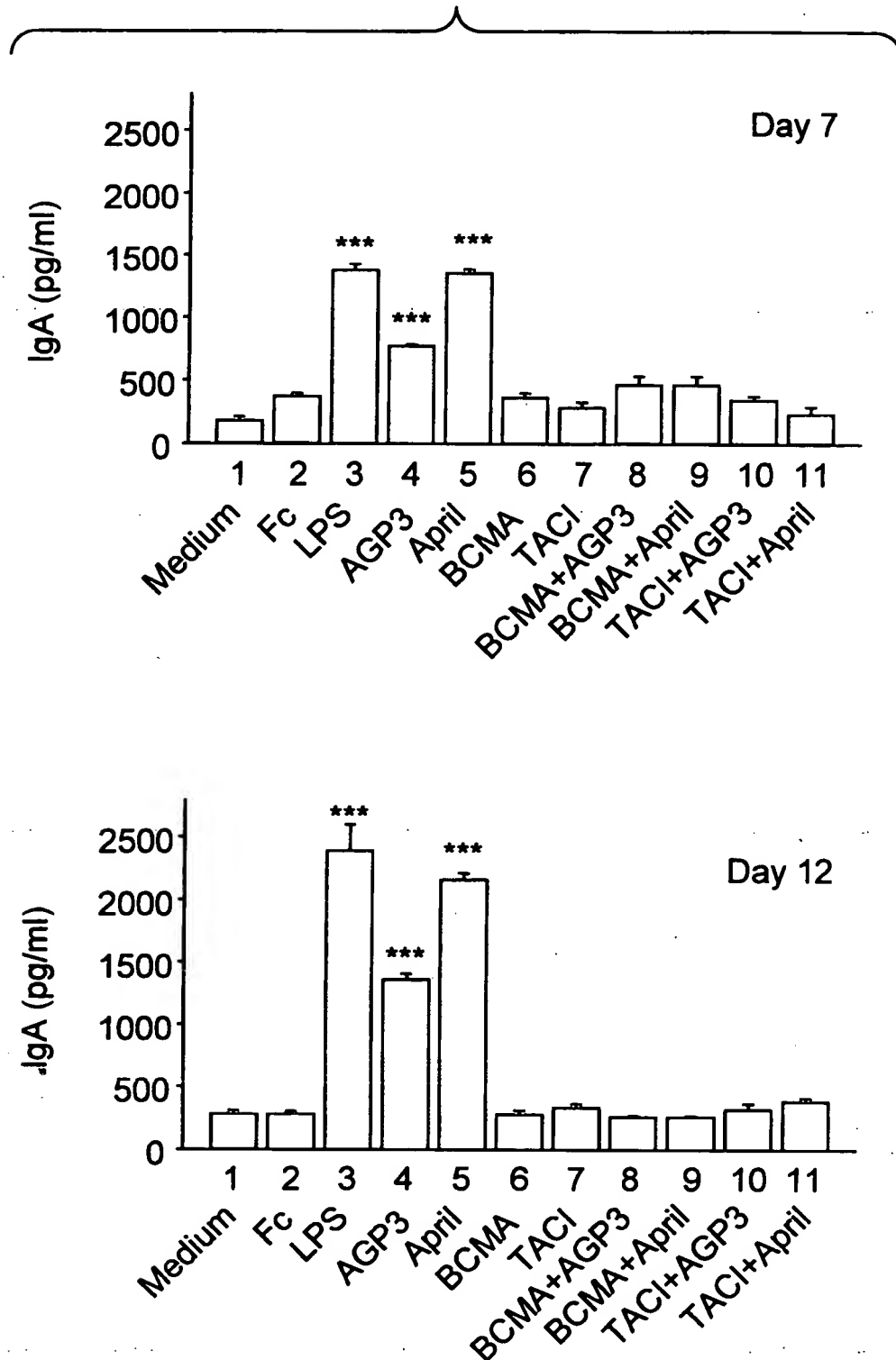


FIG. 27

Flag-mAPRIL and hAGP3 Mediated IgG Production
Inhibited by BCMA-Fc and TACI-Fc *in Vitro*

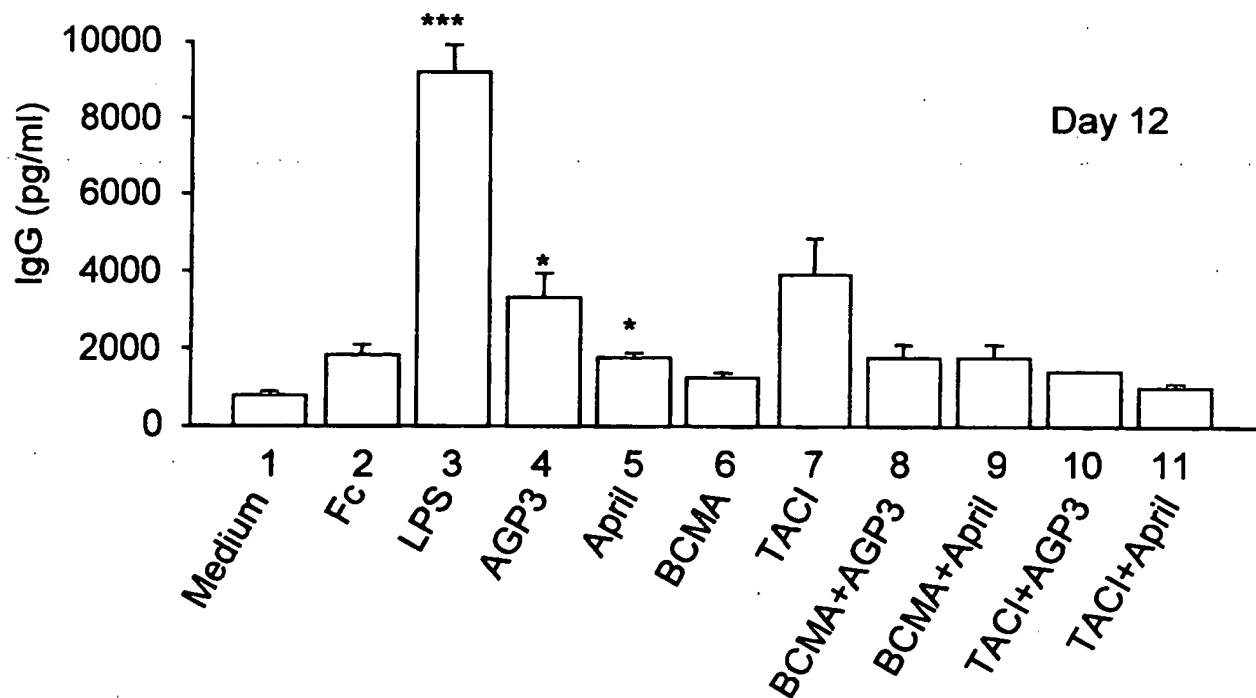
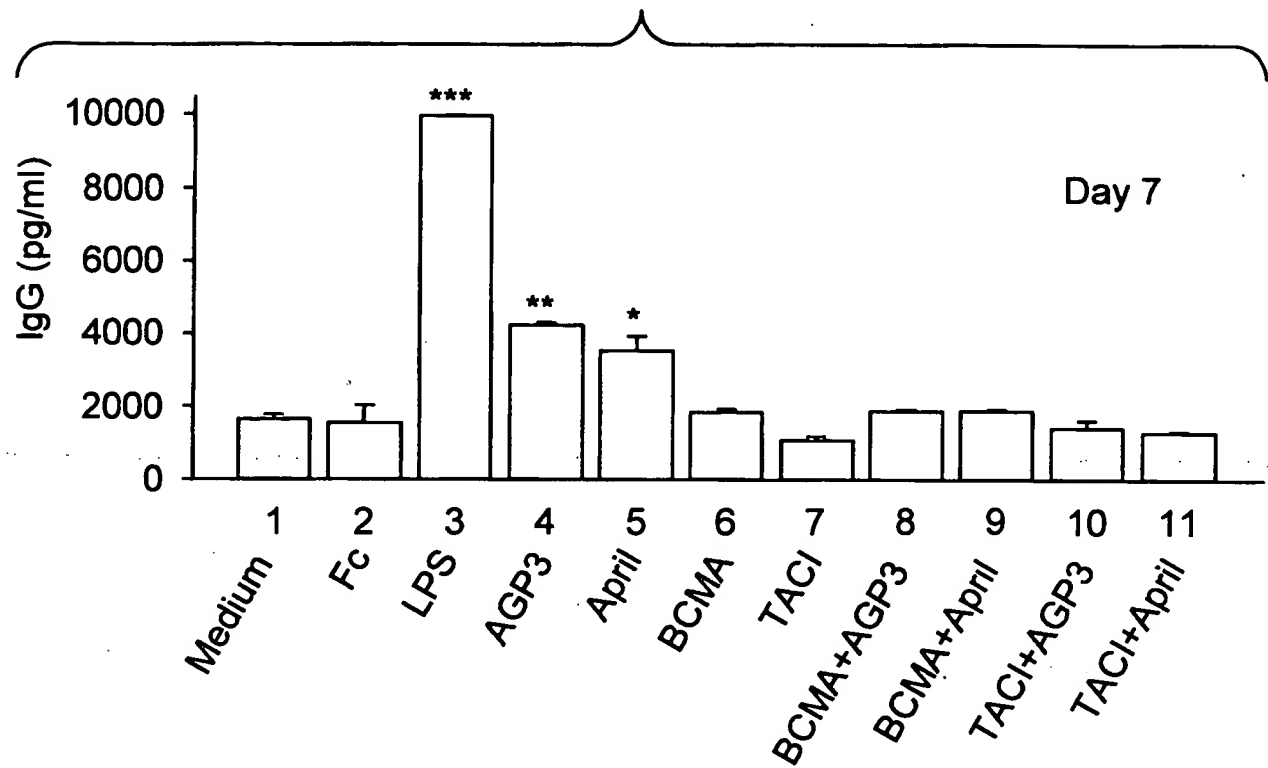


FIG. 28

Significantly reduces total IgE and IgA in normal mice treated with mBCMA-Fc and trun hTACI-Fc 5 mg/kg *ip* day 0, 3, and 6

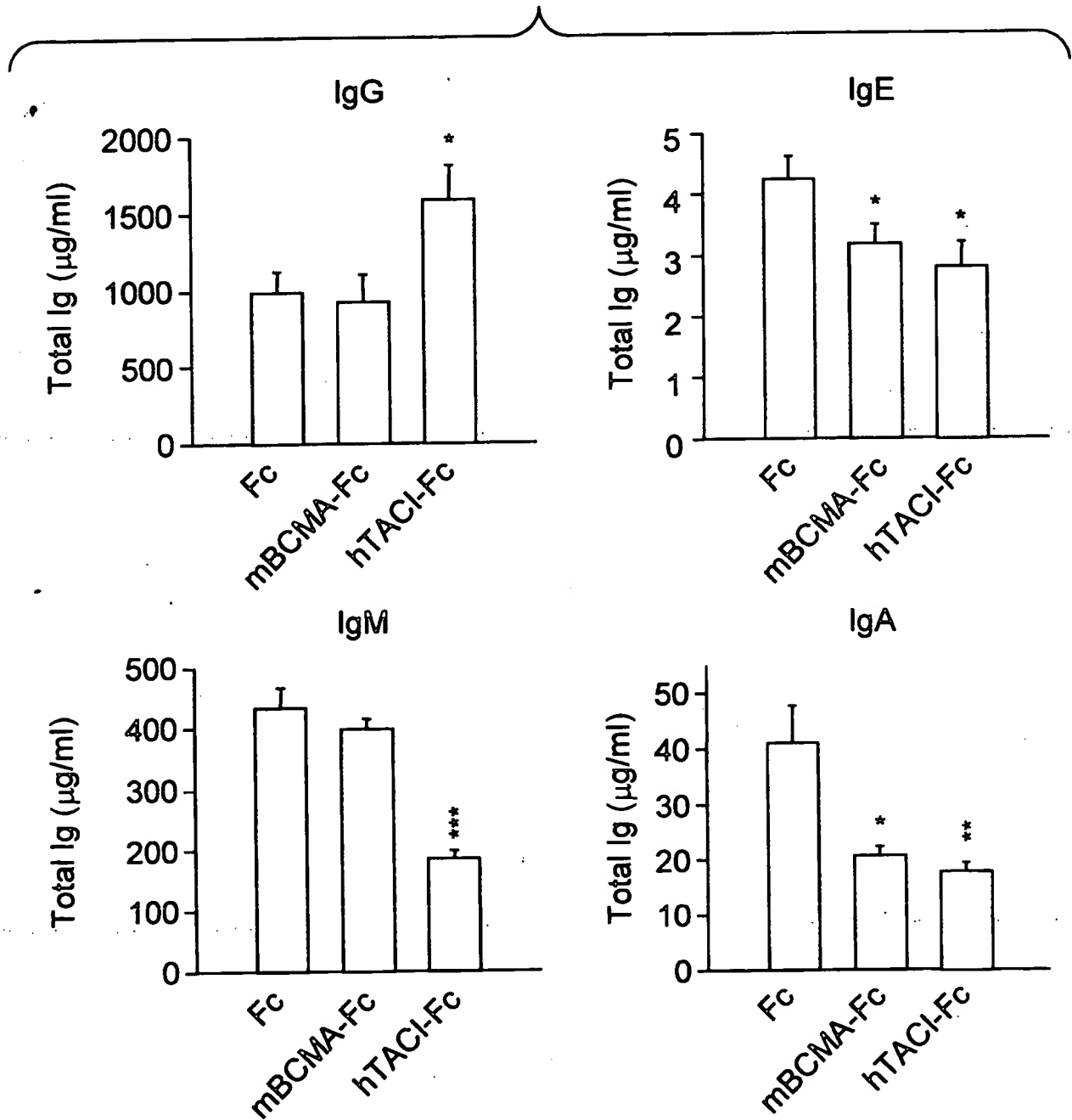


FIG. 29

BCMA-Fc and truncated TACI-Fc at daily doses of 0.5 mg/kg inhibits humoral immunity *in vivo*

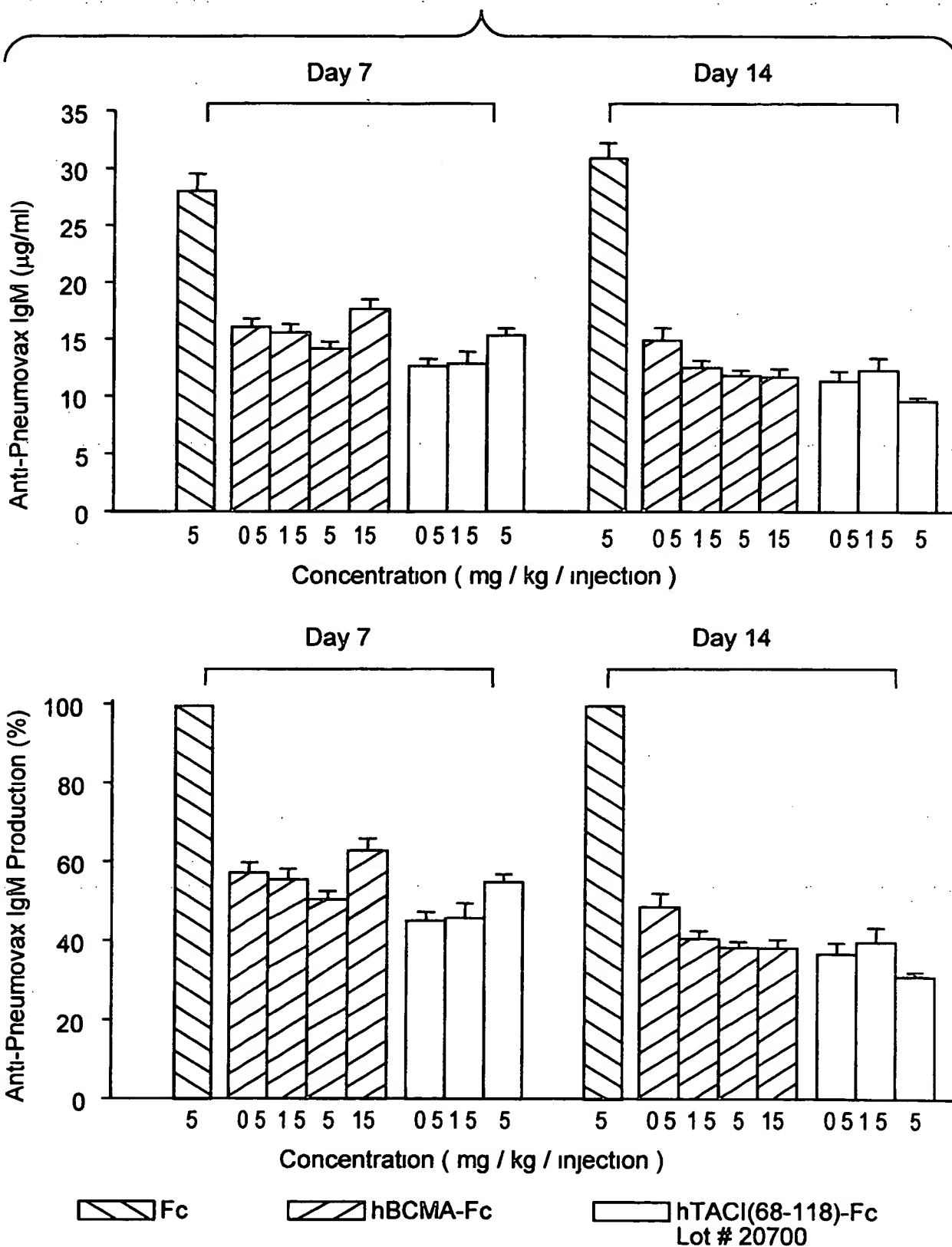


FIG. 30

Anti-mAPRIL c-19 MAb
Inhibition of APRIL mediated B cell proliferation

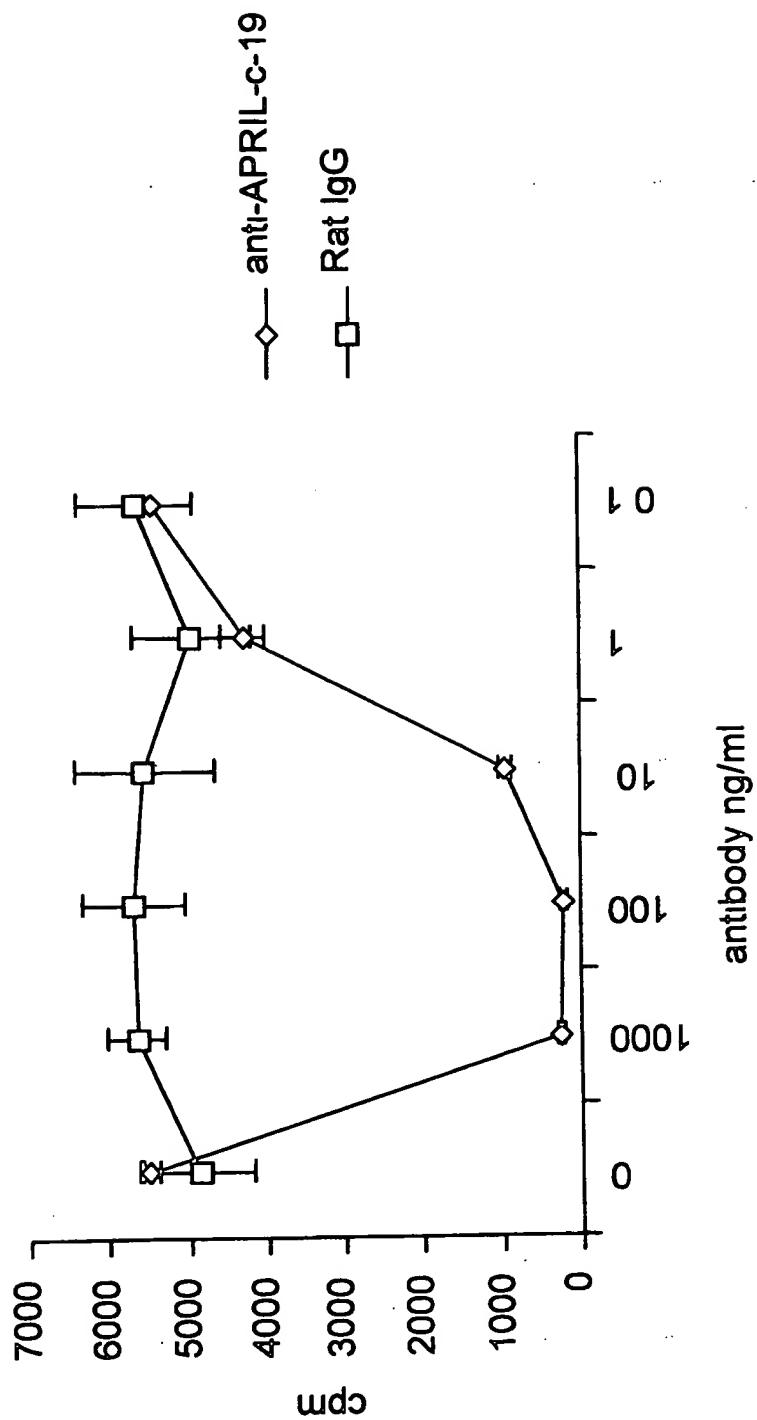
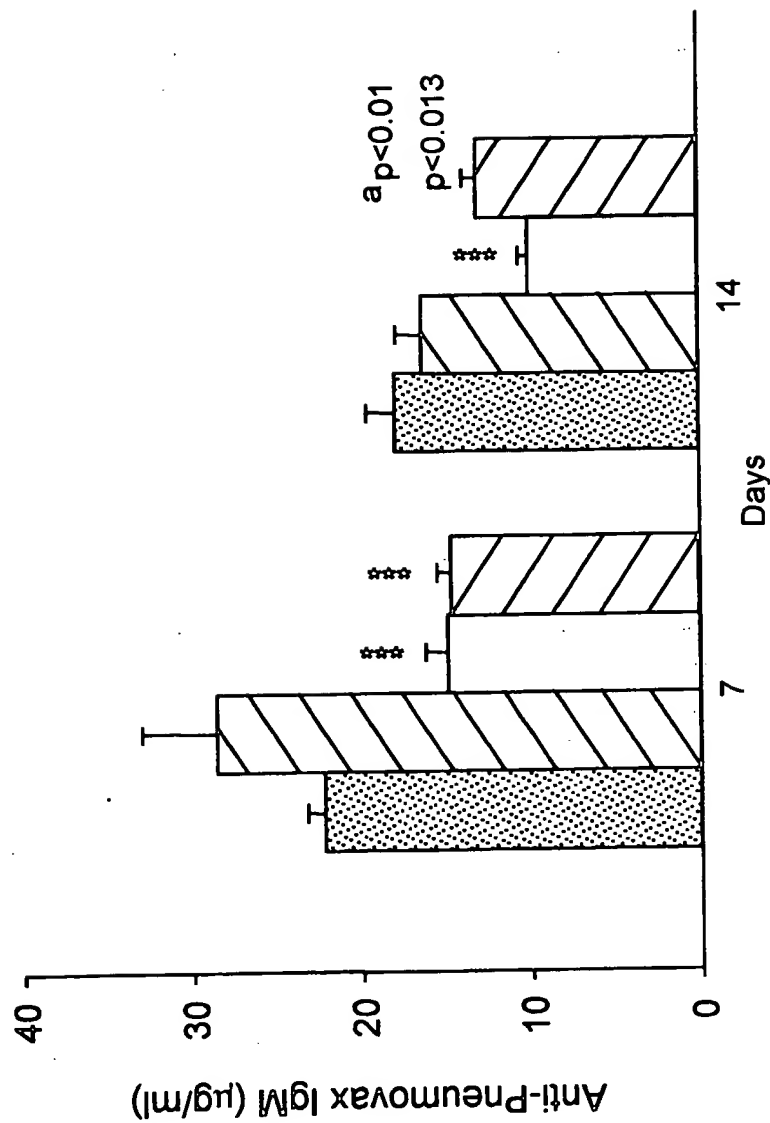


FIG. 31

Neutralizing anti-mAPRIL Mab Reduces anti-Pneumovax IgM *In Vivo*
 5 mg/kg ip on day 0, 3, and 6

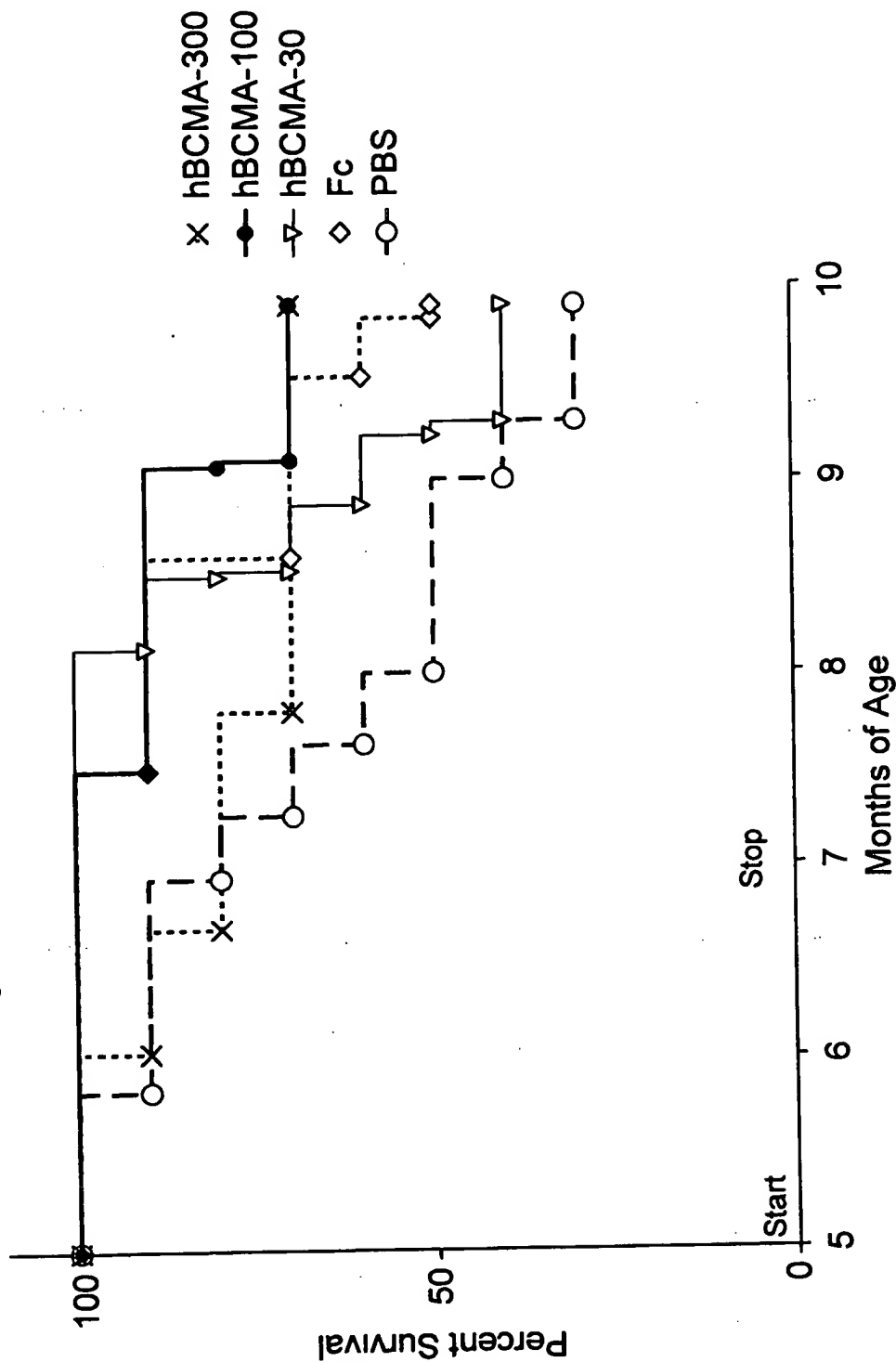
Fc Anti-April Ab
 anti-AGP3 Pb Peak 2 anti-AGP3 Pb Peak 2 + Anti-April Ab



a difference between Anti-April Ab and anti-AGP3 Pb Peak 2 + Anti-April Ab Groups

FIG. 32

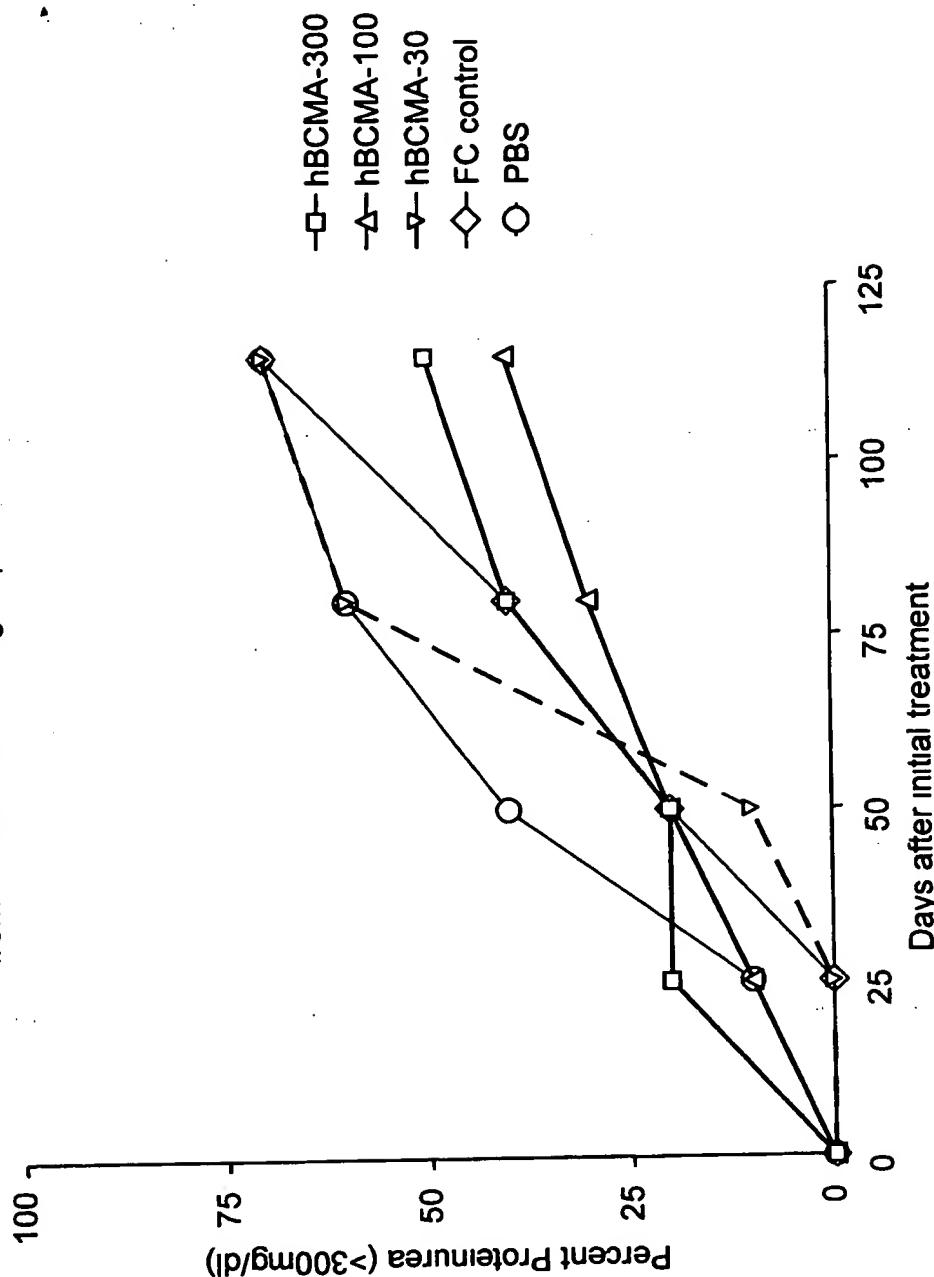
Effect of hBCMA-Fc in NCB/NCWF1 mice
Survival graph from various treatment groups



N=10 Mice were treated for 8 weeks 3x/week with the indicated proteins KIN2 group had 12 mice
The 100 in the legend stands for 100 µg of protein or 4mg/kg i p

FIG. 33

Effect of hBCMA-Fc in NCB/NCWF1 mice
 Percentage of mice with proteinuria (>300mg/dl)
 from various treatment groups



N=10 Five month old BWF1 mice were treated with protein for 8 weeks i p
 The hBCMA-300 stands for hBCMA-fc 300 µg/mouse (12mg/kg)

FIG. 34

Analysis of antibodies to dsDNA from the peripheral blood
from various treatment groups of BWF1 at day 0,30,60, and 90

MEAN anti-dsDNA isotypes in U/ml

Group #	Day 0		Day 30		Day 60		Day 90	
	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
hBCMA-300	179	560	163	371	150	706	171	841
hBCMA-100	150	430	259	718	171	822	339	1031
hBCMA-30	377	592	297	458	401	664	424	601
FC	149	371	234	283	384	331	432	351
PBS	308	292	439	311	247	576	720	467

Standard Deviation of the above means

Group #	Day 0		Day 30		Day 60		Day 90	
	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
hBCMA-300	104	303	116	211	62	518	62	734
hBCMA-100	109	262	306	461	212	758	371	1225
hBCMA-30	363	455	281	430	305	606	421	400
FC	68	160	150	93	391	151	233	237
PBS	311	73	474	152	247	370	870	327

FIG. 35

Evaluation of B cell numbers at treatment day 60 from
the 12mg/kg (30 ug), 4mg/kg (100ug), and 1 3mg/kg (300 ug) dose of
hBCMA-Fc groups along with the Fc and PBS control groups

hBCMA-fc-300					hBCMA-100					hBCMA-Fc-30				
Mouse#	%CD4	%CD8	%B220		%CD4	%CD8	%B220			%CD4	%CD8	%B220		
10	163	110	164		261	149	101		90	25	69	103		
20	241	111	116		211	113	106		100	132	52	234		
30	182	74	99		246	133	83		110	159	64	292		
40	254	133	131		200	113	134		120	148	76	315		
x	210	107	128		230	127	106		x	116	65	236		
sd	44	24	28		sd	17	21		sd	62	10	95		
Fc					PBS									
330	70	81	254		169	83	155							
340	107	49	153		191	121	195							
350	189	93	210		71	34	175							
360	201	111	210		199	114	265							
x	142	84	207		158	88	198							
sd	64	26	41		sd	40	48							

FIG. 36

Specific APRIL binding to Human Cell lines determined by FACS analysis

APRIL binding

HT 29 Colon adenocarcinoma	+	+	+
NCI 460 Lung carcinoma	+	+	+
PC3 Prostate adenocarcinoma	+	+	
C6 Glial carcinoma	+	+	
Raji Burkitt lymphoma	+	+	+
A20 Mouse B cell lymphoma	+	+	+
U266BI Myeloma	+	+	+
A435 Epidermoid carcinoma	--		
A469 Kidney carcinoma	--		
MDA-231 breast adenocarcinoma	--		

FIG. 37

Effect of APRIL, BCMA-Fc and TACI-Fc truncated on U266BI cell proliferation

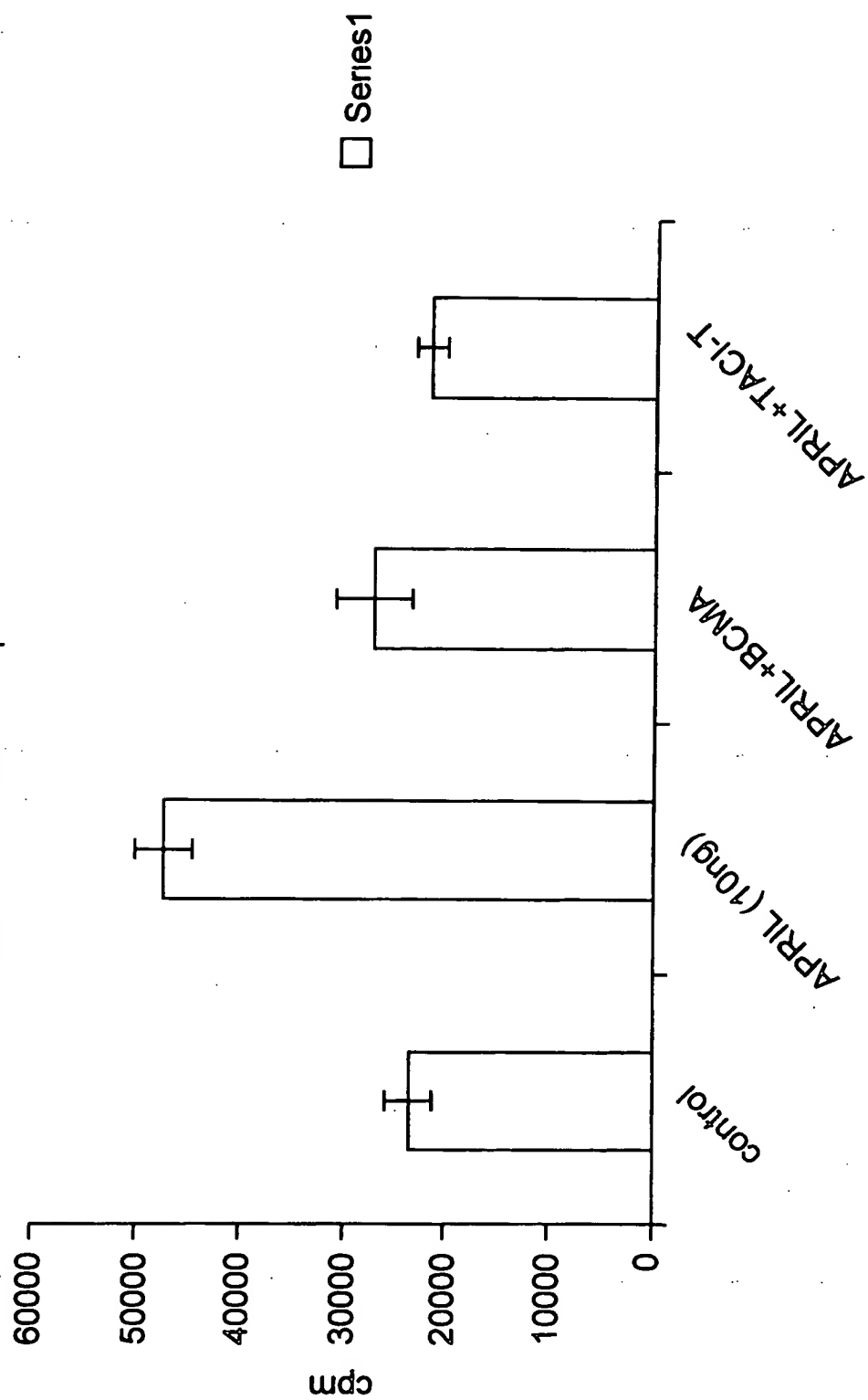


FIG. 38

APRIL and AGP3 stimulates and BCMA-Fc
inhibits B lymphoma cell proliferation

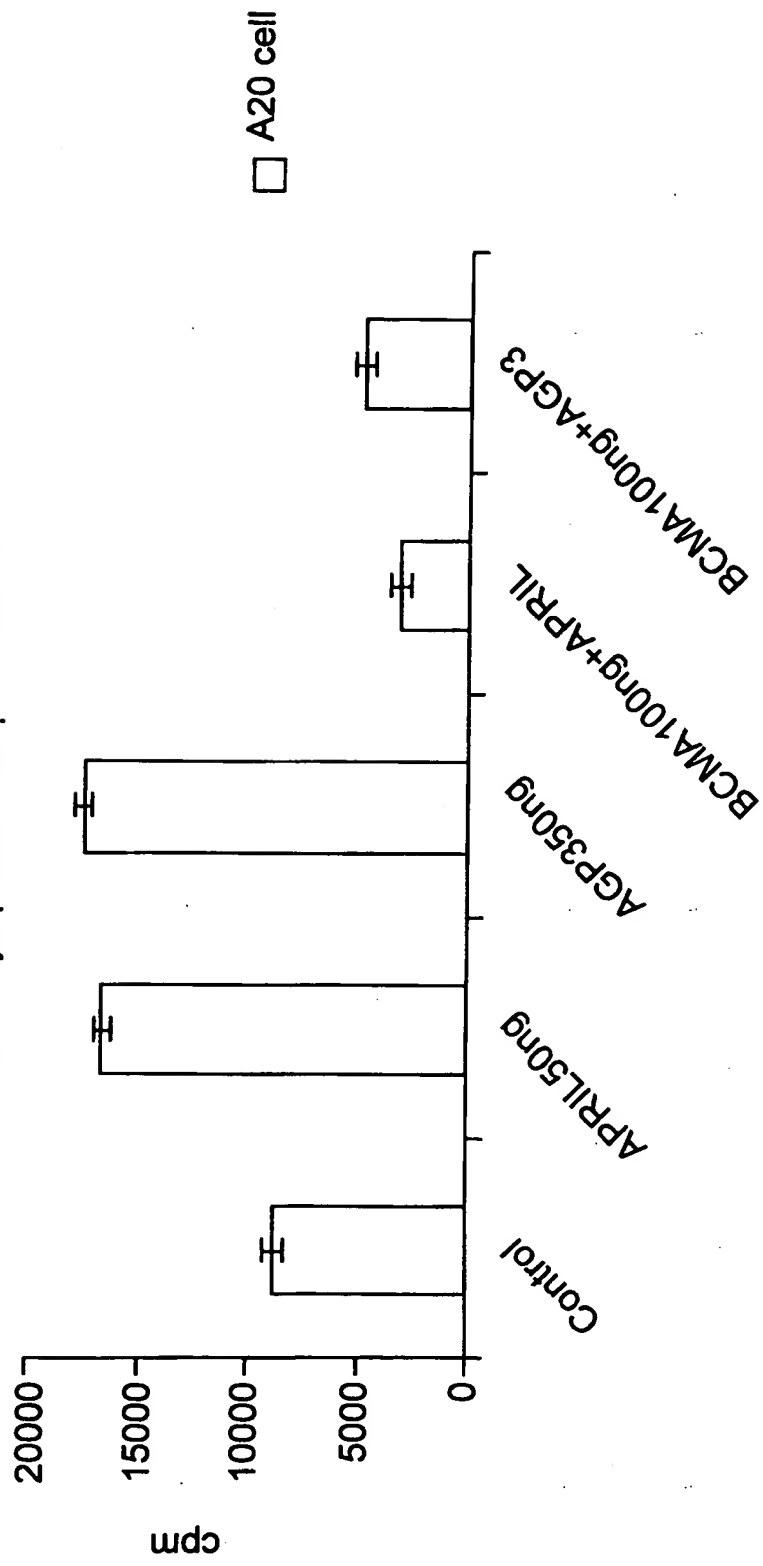


FIG. 39

Effects of BCMA & hTACI on the Growth of A20 in Balb/c Mice

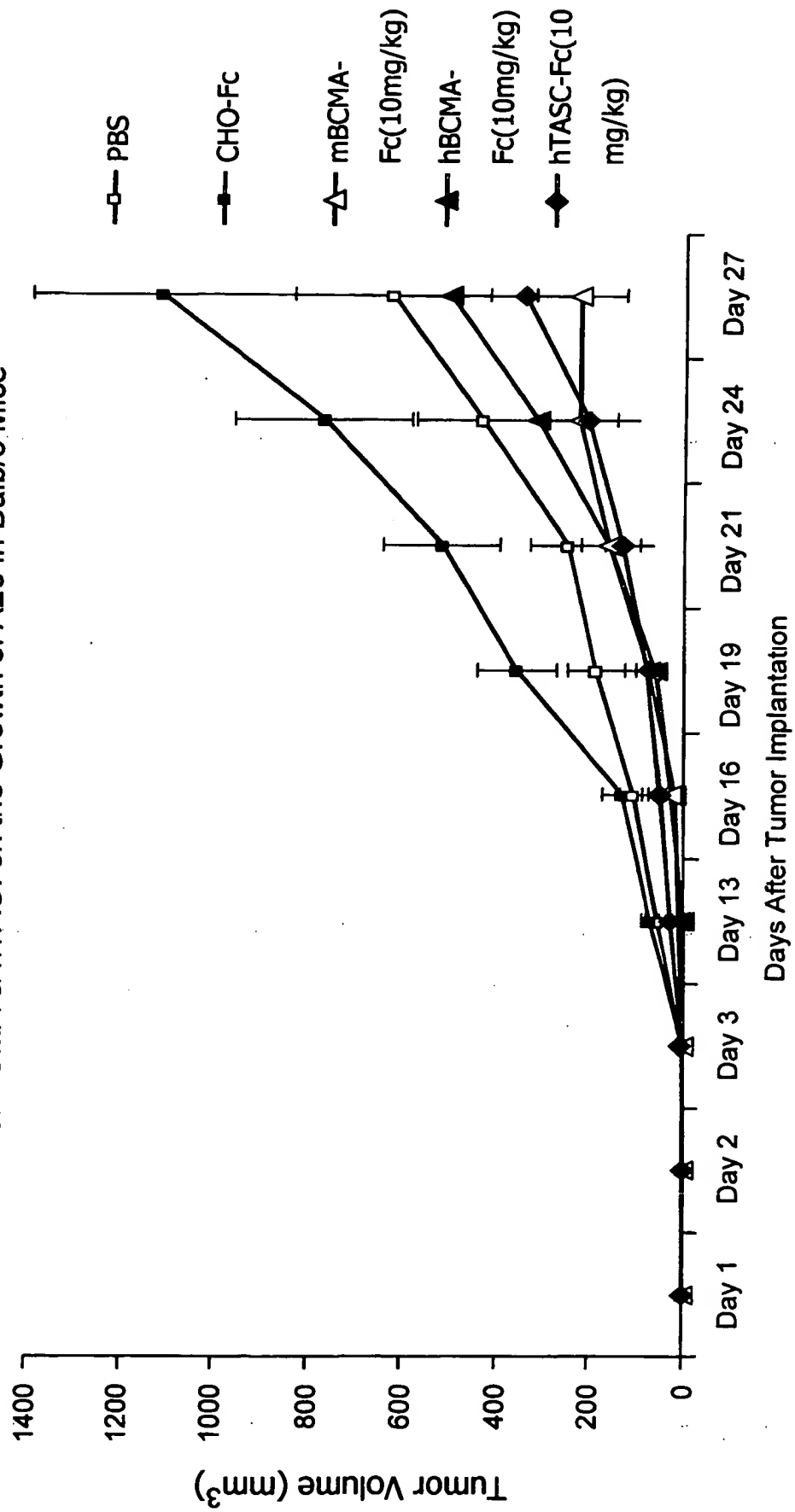
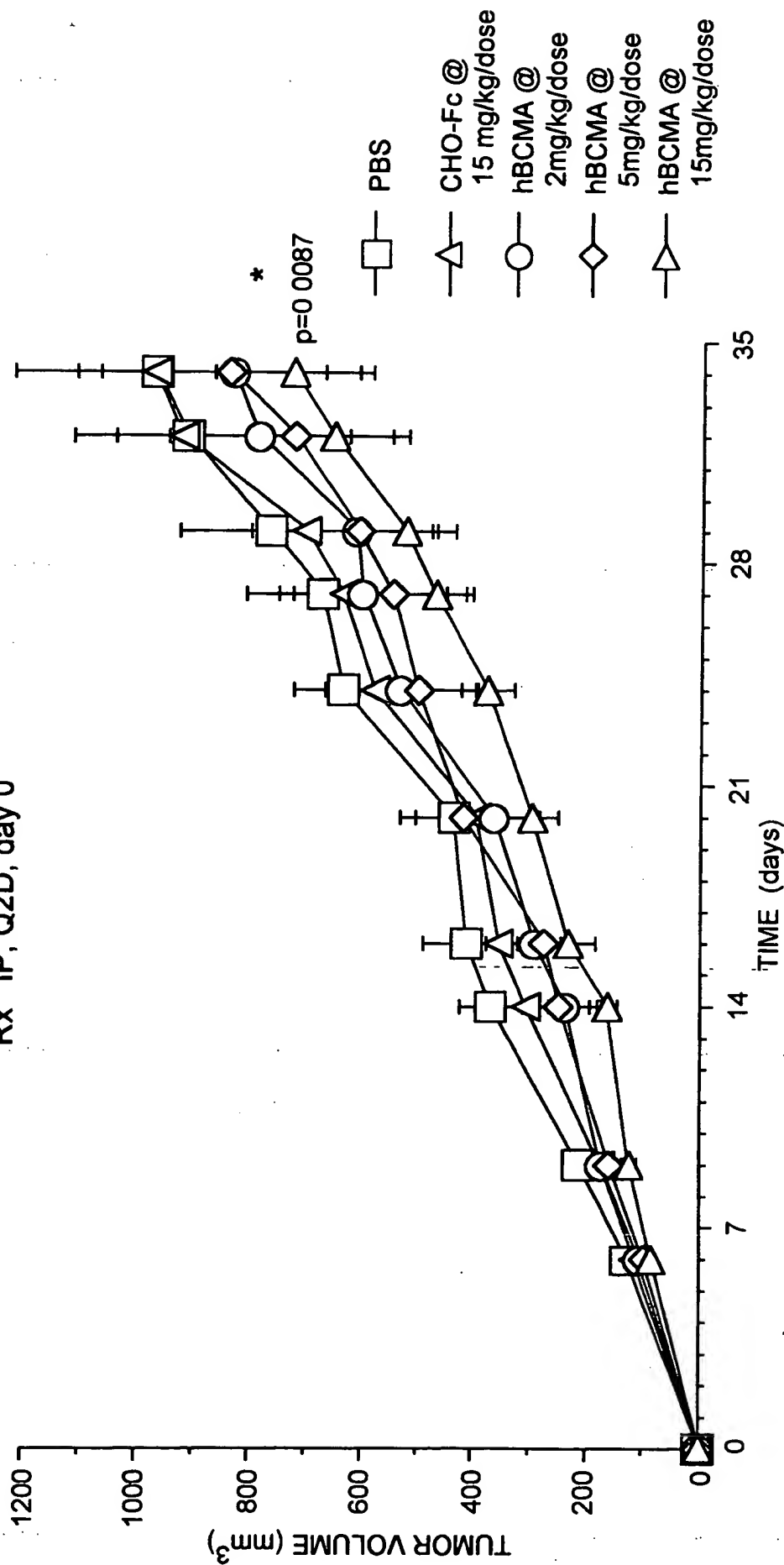


FIG. 40

EFFECT OF HUMAN BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH

Rx IP, Q2D, day 0



* Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)

FIG. 41

EFFECT OF MURINE BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH

Rx IP, Q2D, day 0

